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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	DEC 01	ChemPort single article sales feature unavailable
NEWS 3	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 4	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 5	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS 6	FEB 10	COMPENDEX reloaded and enhanced
NEWS 7	FEB 11	WTEXTILES reloaded and enhanced
NEWS 8	FEB 19	New patent-examiner citations in 300,000 CA/CAplus patent records provide insights into related prior art
NEWS 9	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS 10	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS 11	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS 12	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 13	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS 14	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS 15	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats
NEWS 16	MAR 11	EPFULL backfile enhanced with additional full-text applications and grants
NEWS 17	MAR 11	ESBIOBASE reloaded and enhanced
NEWS 18	MAR 20	CAS databases on STN enhanced with new super role for nanomaterial substances
NEWS 19	MAR 23	CA/CAplus enhanced with more than 250,000 patent equivalents from China
NEWS 20	MAR 30	IMSPATENTS reloaded and enhanced
NEWS 21	APR 03	CAS coverage of exemplified prophetic substances enhanced
NEWS 22	APR 07	STN is raising the limits on saved answers
NEWS 23	APR 24	CA/CAplus now has more comprehensive patent assignee information
NEWS 24	APR 26	USPATFULL and USPAT2 enhanced with patent assignment/reassignment information
NEWS 25	APR 28	CAS patent authority coverage expanded
NEWS 26	APR 28	ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS 27	APR 28	Limits doubled for structure searching in CAS REGISTRY
NEWS 28	MAY 08	STN Express, Version 8.4, now available
NEWS 29	MAY 11	STN on the Web enhanced

```
 NEWS 30  MAY 11  BEILSTEIN substance information now available on
                  STN Easy

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:51:03 ON 13 MAY 2009

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22

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STRUCTURE FILE UPDATES:   12 MAY 2009  HIGHEST RN 1146247-90-6
DICTIONARY FILE UPDATES:  12 MAY 2009  HIGHEST RN 1146247-90-6

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

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REGISTRY includes numerically searchable data for experimental and
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experimental property data in the original document.  For information
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http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10575683d.str
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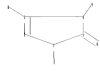


chain nodes :
6 7 8 9
ring nodes :
1 2 3 4 5
chain bonds :
1-7 3-8 4-9 5-6
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 1-7 2-3 3-4 3-8 4-5 4-9 5-6

G1:H,Ak,Cb,NH2,C

G2:H,Cb,Cy,Hy

G3:Cb,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:CLASS 9:CLASS

L1 STRUCTURE UPLOADED

```
=> d l1
L1 HAS NO ANSWERS
L1                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1 full
FULL SEARCH INITIATED 15:51:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      253 TO ITERATE

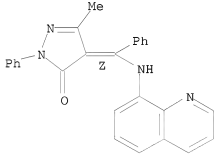
100.0% PROCESSED      253 ITERATIONS                                  6 ANSWERS
SEARCH TIME: 00.00.01

L2             6 SEA SSS FUL L1

=> d l2 1-6

L2   ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   960323-02-8  REGISTRY
ED   Entered STN:  10 Jan 2008
CN   3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl-4-[phenyl(8-
     quinolinylamino)methylene]-, (4Z)-  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C26 H20 N4 O
SR   CA
LC   STN Files:   CA, CAPLUS

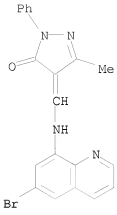
Double bond geometry as shown.
```




```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

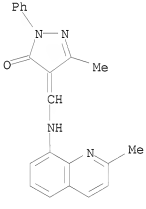
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2   ANSWER 2 OF 6  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   799770-63-1  REGISTRY
ED   Entered STN:  20 Dec 2004
CN   3H-Pyrazol-3-one, 4-[[(6-bromo-8-quinolinyl)amino]methylene]-2,4-dihydro-5-
     methyl-2-phenyl-  (CA INDEX NAME)
MF   C20 H15 Br N4 O
SR   Chemical Library
       Supplier: Interchim
LC   STN Files:   CHEMCATS
```



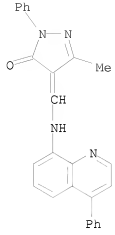
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2009 ACS on STN
RN 796878-42-7 REGISTRY
ED Entered STN: 13 Dec 2004
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-4-[[(2-methyl-8-quinolinyl)amino]methylene]-2-phenyl- (CA INDEX NAME)
MF C21 H18 N4 O
SR Chemical Library
Supplier: Interchim
LC STN Files: CHEMCATS



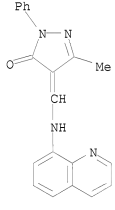
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2009 ACS on STN
RN 796876-81-8 REGISTRY
ED Entered STN: 13 Dec 2004
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl-4-[[(4-phenyl-8-quinolinyl)amino]methylene]- (CA INDEX NAME)
MF C26 H20 N4 O
SR Chemical Library
Supplier: Interchim
LC STN Files: CHEMCATS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2009 ACS on STN
RN 331818-08-7 REGISTRY
ED Entered STN: 19 Apr 2001
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl-4-[(8-quinolinylamino)methylene]- (CA INDEX NAME)
MF C20 H16 N4 O
SR Chemical Library
Supplier: AsInEx
LC STN Files: CHEMCATS

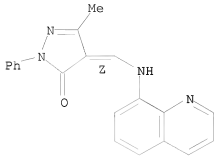


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2009 ACS on STN
RN 313945-30-1 REGISTRY
ED Entered STN: 15 Jan 2001
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl-4-[(8-quinolinylamino)methylene]-, (4Z)- (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H16 N4 O

SR CA
LC STN Files: CA, CAPLUS

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	198.66	198.88

FILE 'CAPLUS' ENTERED AT 15:52:37 ON 13 MAY 2009
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FILE COVERS 1907 - 13 May 2009 VOL 150 ISS 20
FILE LAST UPDATED: 12 May 2009 (20090512/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

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This file contains CAS Registry Numbers for easy and accurate

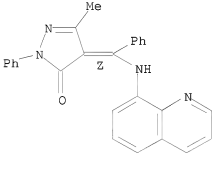
=> s l2
L3 2 L2

```
=> d l2 1-2 ibib abs hitstr
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:n


=> d l3 1-2 ibib abs hitstr

L3   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:          2007:488033  CAPLUS
DOCUMENT NUMBER:           148:89522
TITLE:                     3-Methyl-1-phenyl-4-[phenyl(8-
                           quinolylamino)methylene]pyrazol-5(4H)-one
AUTHOR(S):                 Sun, Yi-Feng; Li, Ji-Kun; Wu, Ren-Tao; Zheng, Ze-Bao
CORPORATE SOURCE:          Department of Chemistry, Taishan University, Shandong,
                           271021, Peop. Rep. China
SOURCE:                    Acta Crystallographica, Section E: Structure Reports
                           Online (2007), E63(5), o2176-o2177
                           CODEN: ACSEBH; ISSN: 1600-5368
                           URL: http://journals.iucr.org/e/issues/2007/05/00/hg22
                           16/hg2216.pdf
PUBLISHER:                 Blackwell Publishing Ltd.
DOCUMENT TYPE:             Journal; (online computer file)
LANGUAGE:                  English
AB   3-Methyl-1-phenyl-4-[phenyl(8-quinolylamino)methylene]pyrazol-5(4H)-one,
     C26H20N4O, was synthesized by the reaction of
     1-phenyl-3-Me-4-benzoylpyrazol-5-one and 8-aminoquinoline.  The mol.
     exists in the enamine-keto tautomeric form.  Crystallog. data are given.
IT   960323-02-8P
     RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
        (preparation and crystal and mol. structure of)
RN   960323-02-8  CAPLUS
CN   3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl-4-[phenyl(8-
     quinolinylamino)methylene]-, (4Z)-  (CA INDEX NAME)

Double bond geometry as shown.
```

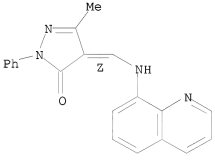



```
REFERENCE COUNT:           10    THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:          2000:778020  CAPLUS
DOCUMENT NUMBER:           134:56333
TITLE:                     Synthesis and IR and NMR spectroscopic studies of
                           amino derivatives of oxo-, thio-, and selenopyrazole.
                           Crystal and molecular structure of
                           1-phenyl-3-methyl-4-[(8-quinolinylamino)methylene]-5-
                           oxopyrazole
AUTHOR(S):                 Antsyshkina, A. S.; Sadikov, G. G.; Uraev, A. I.;
                           Korshunov, O. Yu.; Novorozhkin, A. L.; Garnovskii, A.
```

D.
CORPORATE SOURCE: Inst. Obshch. Neorg. Khim., RAN, Moscow, Russia
SOURCE: Kristallografiya (2000), 45(5), 850-853
CODEN: KRISAJ; ISSN: 0023-4761
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB NMR anal. of the NH group proton revealed that 1-phenyl-3-methyl-4-[(8-quinolinylamino)methylene]-5-(thioxo/selenoxo)pyrazole had the named enamine structure in CDCl3 with a strong intramol. H bond NH...X (X = S, Se). The ketone analog (X = O, I) differed significantly from these: here, the NH proton was engaged in a rapid exchange process. The Z-enamine tautomeric structure of I in the crystalline state was determined by x-ray crystallog.: the NH proton was engaged in a bifurcated H bond, forming fused 6- and 5-membered rings with the ketone O and the quinoline N.
IT 313945-30-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(crystallog.; IR, NMR, and crystallog. studies of the tautomeric structure of 1-phenyl-3-methyl-4-[(8-quinolinylamino)methylene]-5-oxopyrazole and its thioxo and selenoxo analogs)
RN 313945-30-1 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl-4-[(8-quinolinylamino)methylene]-, (4Z)- (CA INDEX NAME)

Double bond geometry as shown.



=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	21.78	220.66
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.64	-1.64

FILE 'REGISTRY' ENTERED AT 16:05:20 ON 13 MAY 2009
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STRUCTURE FILE UPDATES: 12 MAY 2009 HIGHEST RN 1146247-90-6
DICTIONARY FILE UPDATES: 12 MAY 2009 HIGHEST RN 1146247-90-6

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10575683d.str

chain nodes :
6 7 8 9
ring nodes :
1 2 3 4 5
chain bonds :
1-7 3-8 4-9 5-6
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :

1-2 1-5 1-7 2-3 3-4 3-8 4-5 4-9 5-6

G1:H,Ak,Cb,NH2,C

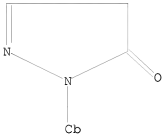
G2:H,Cb,Cy,Hy

G3:Cb,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:CLASS 9:CLASS

L4 STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4 STR



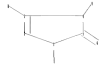
Structure attributes must be viewed using STN Express query preparation.

=> s l4 full
FULL SEARCH INITIATED 16:05:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 504145 TO ITERATE

100.0% PROCESSED 504145 ITERATIONS 71617 ANSWERS
SEARCH TIME: 00.00.11

L5 71617 SEA SSS FUL L4

=>
Uploading C:\Program Files\Stnexp\Queries\10575683d.str



chain nodes :
6 7 8 9
ring nodes :
1 2 3 4 5
chain bonds :
1-7 3-8 4-9 5-6
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 1-7 2-3 3-4 3-8 4-5 4-9 5-6

G1:H,Ak,Cb,NH2,C

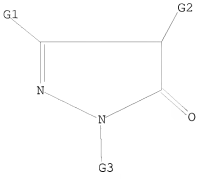
G2:H,Cb,Cy,Hy

G3:Cb,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:CLASS 9:CLASS

L6 STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6 STR



G1 H,Ak,Cb,NH2,C

G2 H,Cb,Cy,Hy

G3 Cb,H

Structure attributes must be viewed using STN Express query preparation.

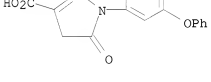
=> s l6 full
FULL SEARCH INITIATED 16:14:19 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 504145 TO ITERATE

100.0% PROCESSED 504145 ITERATIONS 24092 ANSWERS
SEARCH TIME: 00.00.10

L7 24092 SEA SSS FUL L6

=> d scan

L7 24092 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN 1H-Pyrazole-3-carboxylic acid, 4,5-dihydro-5-oxo-1-(3-phenoxyphenyl)-
MF C16 H12 N2 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

FULL ESTIMATED COST	378.48	599.14
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.64

FILE 'CAPLUS' ENTERED AT 16:15:04 ON 13 MAY 2009
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FILE COVERS 1907 - 13 May 2009 VOL 150 ISS 20
FILE LAST UPDATED: 12 May 2009 (20090512/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate

```
=> s l7
L8       18988 L7

=> s l8 and neutrophil
         55121 NEUTROPHIL
L9          28 L8 AND NEUTROPHIL

=>
=> d l9 1-28 ibib abs hitstr
```

L9 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2008:1405251 CAPLUS
DOCUMENT NUMBER:	150:389963
TITLE:	Combination drug therapy using edaravone and Daio-Orengedoku-to after transient focal ischemia in rats
AUTHOR(S):	Cho, K.-H.; Oh, J. K.; Jang, Y. S.; Jung, J. W.; Oh, H. R.; Park, E.-K.; Kim, D. H.; Moon, S.-K.; Kim, D.-H.; Ryu, J. H.
CORPORATE SOURCE:	College of Oriental Medicine, Kyung Hee University, Seoul, S. Korea
SOURCE:	Methods and Findings in Experimental and Clinical Pharmacology (2008), 30(6), 443-450 CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER:	Prous Science
DOCUMENT TYPE:	Journal

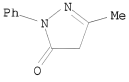
LANGUAGE: English

AB In this study, we investigated the effect of Daio-Orengedoku-to (DOT) on ischemic brain damage in a rat model of focal ischemia-reperfusion and attempted to identify synergistic effects for the combination of edaravone and DOT against ischemic insult. Ischemia was induced by intraluminal occlusion of the right middle cerebral artery for 2 h and reperfusion followed for 22 h. To determine the neuroprotective effect of DOT, it was administered orally just before reperfusion and then 2 h after reperfusion. To examine the effects of combination therapy on survival, rats were divided into groups treated with edaravone, DOT, and edaravone and DOT. Microglial activation, neutrophil infiltration and brain-derived neurotrophic factor (BDNF) expression were examined in surviving animals. Infarct volume was significantly reduced by DOT (100, 200 and 400 mg/kg; $P < 0.05$), and edaravone plus DOT markedly improved the survival rate after transient ischemia ($P = 0.0133$). Microglial activation was reduced by edaravone and DOT and their combination ($P < 0.05$), and neutrophil infiltration was lowered in these groups ($P < 0.05$). BDNF-pos. cells were increased in the combination edaravone and DOT group ($P < 0.05$). It appears that the neuroprotective mechanisms of combined therapy involve inhibition of microglial activation, reduction of invading neutrophils and enhancement of BDNF expression.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination drug therapy using edaravone and Daio-Orengedoku-to after transient focal ischemia in rats)

RN 89-25-8 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:932720 CAPLUS

DOCUMENT NUMBER: 150:229507

TITLE: Research on the effect of sivelestat sodium on astrocytes in ischemia/reperfusion injury

AUTHOR(S): Li, Man-Xia; Dong, Zhi

CORPORATE SOURCE: Chongqing Medical University, Chongqing, 400016, Peop. Rep. China

SOURCE: Jiefangjun Yaoxue Xuebao (2008), 24(3), 195-198
CODEN: JYXIAY; ISSN: 1008-9926

PUBLISHER: Zhongguo Renmin Jiefangjun Zonghouqinbu Weishengbu Yaopin Yiqi Jianyansuo

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

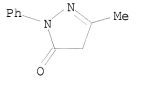
AB The objective of the paper is to study the protective effect of the sivelestat sodium on astrocytes damaged by ischemia/reperfusion. The results were determined by the MTT assay, LDH kit and AQP4 expression in culture astrocytes damaged ischemia-reperfusion by hypoxia-reoxygenation. The results showed that the compared with ischemic group and ischemia+ neutrophil injury group, sivelestat sodium can significantly improve the protective effect on damage of isolated astrocytes and there

was a dose-effect relationship between the 1 + 10-8 to 1 + 10-6 mol/L-1 concns. It was concluded that the NE inhibitor sivelestat sodium plays a protective role in astrocytes ischemic injury.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of sivelestat sodium on astrocytes in ischemia/reperfusion injury)

RN 89-25-8 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



L9 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:931977 CAPLUS

DOCUMENT NUMBER: 150:160008

TITLE: Effects of free radical scavenger on acute liver injury induced by D-galactosamine and lipopolysaccharide in rats

AUTHOR(S): Ito, Koji; Ozasa, Hisashi; Noda, Yumi; Arii, Shigeki; Horikawa, Saburo

CORPORATE SOURCE: Department of Hepato-Biliary-Pancreatic Surgery, Graduate School of Medicine, Medical Research Institute, Tokyo Medical and Dental University, Tokyo, Japan

SOURCE: Hepatology Research (2008), 38(2), 194-201
CODEN: HPRSFM; ISSN: 1386-6346

PUBLISHER: Blackwell Publishing Asia Pty Ltd.

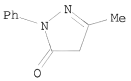
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Aim: Acute severe liver injury still has a high mortality rate. Acute liver injury induced by a coadministration of D-galactosamine (GalN) and lipopolysaccharide (LPS) is an exptl. model of fulminant hepatitis in rats. Our aim is to investigate the effects of free radical scavenger on the injury induced by GalN/LPS in rats. Methods: Free radical scavenger edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one) was twice injected into rats 5 min before and 60 min after the GalN/LPS injection. Liver injury was biochem. and histol. assessed. The survival rate was examined 72 h after the intoxication. Results: In the GalN/LPS-treated rats, a marked elevation in serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels was observed On the other hand, edaravone significantly inhibited the elevation in serum AST and ALT levels. The efficacy of edaravone was also confirmed by histol. anal. Edaravone lowered the levels of proinflammatory cytokines TNF-α mRNA and interleukin-6 mRNA expression, antioxidative enzyme heme oxygenase-1 protein and myeloperoxidase activity, a marker of neutrophil infiltration, in rat livers. In addition, edaravone reduced the mortality rate in GalN/LPS-treated rats as compared to the rats without edaravone treatment. Conclusions: Free radical scavenger edaravone effectively ameliorated the liver injury induced by the GalN/LPS administration in rats, not only by attenuating oxidative stress, but also by reducing the expression of proinflammatory cytokines.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

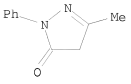
(Biological study); USES (Uses)
(effect of edaravone on fulminant hepatitis in rats)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

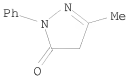
L9 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:106235 CAPLUS
DOCUMENT NUMBER: 149:29532
TITLE: Amelioration of hepatic ischemia/reperfusion injury in the remnant liver after partial hepatectomy in rats
AUTHOR(S): Hiranuma, Susumu; Ito, Koji; Noda, Yumi; Ozasa, Hisashi; Koike, Yuichi; Horikawa, Saburo
CORPORATE SOURCE: Department of Surgery, Tsuchiura Kyodo General Hospital, Ibaraki, Japan
SOURCE: Journal of Gastroenterology and Hepatology (2007), 22(12), 2167-2172
CODEN: JGHEEO; ISSN: 0815-9319
PUBLISHER: Blackwell Publishing Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reactive oxygen species have been implicated in the development of hepatic ischemia/reperfusion (I/R) injury. I/R injury remains an important problem in massive hepatectomy and organ transplantation. The aim of this study was to examine the effect of edaravone, a newly synthesized free radical scavenger, on I/R injury in the remnant liver after partial hepatectomy in rats. Partial (70%) hepatic ischemia was induced in rats by occluding the hepatic artery, portal vein, and bile duct to left and median lobes of liver. Total hepatic ischemia (Pringle maneuver) was induced by occluding the hepatoduodenal ligament. Edaravone was i.v. administered to rats just before reperfusion and partial (70%) hepatectomy was performed just after reperfusion. Edaravone significantly reduced the increases in the levels of serum alanine aminotransferase and aspartate aminotransferase in rats with liver injury induced by 90-min of partial ischemia followed by 120-min of reperfusion. Histopathol. anal. showed that edaravone prevented inflammatory changes in the livers with I/R injury. Edaravone also decreased the levels of myeloperoxidase activity, which is an index of neutrophil infiltration, and interleukin-6 mRNA, which is a proinflammatory cytokine. Addnl., edaravone improved the survival rate in partial hepatectomy rats with I/R injury induced by the Pringle maneuver. Edaravone administration prior to reperfusion protected the liver against I/R injury. Edaravone also improved the function of the remnant liver with I/R injury after partial hepatectomy. Therefore, edaravone may have applicability for major hepatectomy and liver transplantation in the clin. setting.
IT 89-25-8, Edaravone
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ameliorative effects of edaravone on hepatic ischemia/reperfusion injury in remnant liver after partial hepatectomy in rats)
RN 89-25-8 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



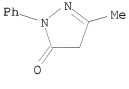
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1094108 CAPLUS
DOCUMENT NUMBER: 149:347363
TITLE: Effects of MCI-186 upon neutrophil-derived active oxygens
AUTHOR(S): Sumitomo, K.; Shishido, N.; Aizawa, H.; Hasebe, N.; Kikuchi, K.; Nakamura, M.
CORPORATE SOURCE: Nakatombetsu National Health Insurance Hospital, Nakatombetsu, Japan
SOURCE: Redox Report (2007), 12(4), 189-194
CODEN: RDRPE4; ISSN: 1351-0002
URL: http://docserver.ingentaconnect.com/deliver/connect/maney/13510002/v12n4/s4.pdf?expires=1190215577&id=39531511&titleid=3971&accname=Theodore+Simos&checksum=61436D494B88B3D7E8B1759E006DD423
PUBLISHER: Maney Publishing
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Reactions of 3-methyl-1-phenyl-2-pyrazoline-5-one (MCI-186) with hypochlorous acid and superoxide were analyzed by spectrophotometry and mass spectrometry. The results were applied to the neutrophil system to evaluate the scavenging activity of neutrophil-derived active oxygen species by MCI-186. MCI-186 reacted rapidly with hypochlorous acid (1 + 106 M-1s-1) to form a chlorinated intermediate, followed by a slow conversion to a new spectrum. MCI-186 consumed 3 mol of hypochlorous acid and did not react with superoxide. The newly synthesized fluorescence probes, 2-[6-(4'-amino)phenoxy-3H-xanthen-3-on-9-yl]benzoic acid (APF) and 2-[6-(4'-hydroxy)phenoxy-3H-anthen-3-on-9-yl]benzoic acid (HPF) successfully detected neutrophil-derived active oxygens. The rate consts. for the reaction of hypochlorous acid with MCI-186 and fluorescence probes was in the order of MCI-186 > APF > HPF. Fluorescence due to the oxidation of APF and HPF was observed with the stimulated neutrophils. The result that the intensity from APF oxidation was higher than that from HPF oxidation is compatible with reports that APF selectively reacts with hypochlorous acid. Fluorescence due to oxidation of both APF and HPF decreased when the reactions were carried out in the presence of a fluorescence probe and MCI-186 in a dose-dependent manner. These results indicate that MCI-186 effectively scavenges neutrophil-derived hypochlorous acid and other active oxygens.
IT 89-25-8, MCI-186
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of MCI-186 upon neutrophil-derived active oxygens)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:255410 CAPLUS
DOCUMENT NUMBER: 146:288299
TITLE: Effects of edaravone on singlet oxygen released from activated human neutrophils. [Erratum to document cited in CA146:220947]
AUTHOR(S): Sommani, Piyanart; Arai, Toshiyuki; Yamashita, Kouhei; Miyoshi, Takashi; Mori, Hiroko; Sasada, Masataka; Makino, Keisuke
CORPORATE SOURCE: School of Health Science, Faculty of Medicine, Kyoto University, Kyoto, 606-8507, Japan
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2007), 103(2), 252
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page 117, the institutional affiliation of the sixth author was incorrectly shown because the wrong affiliation reference number was inserted. The corrected affiliation reference for this author should read as follows: "School of Health Science, Faculty of Medicine, Kyoto University, Kyoto 606-8507, Japan".
IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(edaravone on singlet oxygen released from activated human neutrophils (Erratum))
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



L9 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:195499 CAPLUS
DOCUMENT NUMBER: 146:220947
TITLE: Effects of edaravone on singlet oxygen released from activated human neutrophils
AUTHOR(S): Sommani, Piyanart; Arai, Toshiyuki; Yamashita, Kouhei; Miyoshi, Takashi; Mori, Hiroko; Sasada, Masataka; Makino, Keisuke
CORPORATE SOURCE: Institute of Advanced Energy, Kyoto University, Uji, 611-0011, Japan

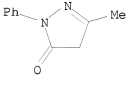
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2007), 103(1), 117-120
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of edaravone, a curative agent for acute brain infarction, on singlet oxygen (1O2) released from activated human neutrophils were examined, and the effects were compared to those of histidine, a 1O2 singlet oxygen scavenger. The neutrophils, stimulated with opsonized zymosan, released 1O2 that was detected by chemiluminescence using a 1O2 specific probe, trans-1-(2'-methoxyvinyl)pyrene. Edaravone dose-dependently suppressed the 1O2 release with an IC50 of approx. 0.3 μM, while the IC50 of histidine was approx. 1 mM. This 1O2 scavenging activity of edaravone might be involved in its curative effects on acute brain infarction.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(edaravone on singlet oxygen released from activated human neutrophils)

RN 89-25-8 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:120401 CAPLUS
DOCUMENT NUMBER: 146:288108
TITLE: The specific free radical scavenger edaravone suppresses bleomycin-induced acute pulmonary injury in rabbits
AUTHOR(S): Asai, Toshihiro; Ohno, Yasushi; Minatoguchi, Shinya; Funaguchi, Norihiko; Yuhgetsu, Hideyuki; Sawada, Masahiro; Takemura, Genzou; Komada, A.; Fujiwara, Takako; Fujiwara, Hisayoshi
CORPORATE SOURCE: Second Department of Internal Medicine, Regeneration and Advanced Medical Science, Graduate School of Medicine, Gifu University, Gifu, Japan
SOURCE: Clinical and Experimental Pharmacology and Physiology (2007), 34(1/2), 22-26
CODEN: CEXPB9; ISSN: 0305-1870
PUBLISHER: Blackwell Publishing Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

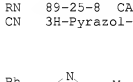
AB Intratracheal instillation of bleomycin induces a condition in rabbits that serves as a useful model of human pulmonary fibrosis. Bleomycin-induced production of reactive oxygen species leads to acute lung inflammation and induction of apoptosis, which is followed by pulmonary fibrosis at a later chronic stage. In the present study, we tested whether edaravone, a free radical scavenger, would suppress bleomycin-induced acute pulmonary inflammation. Rabbits were divided into three groups (n = 10 in each): (i) a bleomycin-treated group, which

received intratracheal instillation of 2 mg/kg bleomycin; (ii) a bleomycin + edaravone group, which received a 10 day regimen of daily i.v. injections of edaravone (3 mg/kg per day) beginning 3 days before bleomycin instillation; and (iii) a saline control group. Rabbits were killed for anal. 7 days after bleomycin administration. In lung tissues from the bleomycin-treated group, marked infiltration of inflammatory cells, consisting mainly of lymphocytes, neutrophils and eosinophils, was observed In addition, significantly increased nos. of TUNEL-pos. (apoptotic) and transforming growth factor-β-pos. cells were seen. All these effects were significantly attenuated by treatment with edaravone. The findings of the present study suggest that edaravone may be useful in the prevention of acute lung injury resulting from the production of reactive oxygen species.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(edaravone suppresses bleomycin-induced acute pulmonary injury)

RN 89-25-8 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1297702 CAPLUS

DOCUMENT NUMBER: 146:330739

TITLE: Edaravone reduces ischemia-reperfusion injury mediators in rat liver

AUTHOR(S): Taniguchi, Masanobu; Uchinami, Masaru; Doi, Koji; Yoshida, Makoto; Sasaki, Hisashi; Tamagawa, Koji; Horiuchi, Tetsuya; Tanaka, Kuniyoshi

CORPORATE SOURCE: Second Department of Surgery, Faculty of Medical Sciences, University of Fukui, Fukui, Japan

SOURCE: Journal of Surgical Research (2007), 137(1), 69-74 CODEN: JSGRA2; ISSN: 0022-4804

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

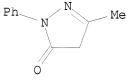
LANGUAGE: English

AB In hepatic ischemia-reperfusion (I/R) injury, oxidative stress both directly injures the liver and promotes an inflammatory reaction by up-regulating various inflammatory mediators. We investigated whether edaravone, a new hydroxy radical scavenger, could reduce hepatic I/R injury including expression of inflammatory mediators such as cytokines and adhesion mols. Male Sprague-Dawley rats were subjected to 30 min of partial hepatic pedicle clamping (70%) followed by reperfusion. Just after initiation of reperfusion and again 1 h later, edaravone was administered intraportally. After reperfusion hepatic lipid peroxidn. was measured by thiobarbituric acid assay, and hepatic injury was quantified by measuring hepatic enzymes in plasma. We serially quantified hepatic expression of mRNAs for tumor necrosis factor (TNF)-α and E-selectin, and histol. examined E-selectin expression and neutrophil accumulation. In the edaravone group, hepatic lipid peroxidn. and hepatic enzyme leakage were significantly less than in the

saline group. Hepatic expression of TNF-α and E-selectin mRNAs was significantly lower in the edaravone than the saline group, at 2 h after initiation of reperfusion. Histol., E-selectin immunoreactivity and neutrophil accumulation were less evident in hepatic sections from the edaravone group. Edaravone reduced hepatic I/R injury by minimizing oxidative stress, and inhibited subsequent injurious inflammation by reducing expression of inflammatory cytokines and adhesion mols.

IT 89-25-8, Edaravone
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(edaravone reduced hepatic ischemia-reperfusion injury by minimizing oxidative stress and inhibited subsequent injurious inflammation by reducing expression of inflammatory cytokines and adhesion mols. in rat liver)

RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

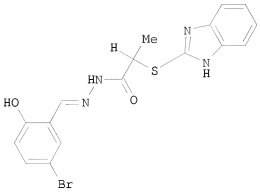
L9 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1118848 CAPLUS
DOCUMENT NUMBER: 145:449207
TITLE: Chemical inhibitors of neutrophil activation through the soluble adenyl cyclase-dependent pathway, and use for the treatment of inflammatory disorders
INVENTOR(S): Nathan, Carl F.; Buck, Jochen; Levin, Lonny R.; Han, Hyunsil
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006113236	A2	20061026	WO 2006-US13537	20060412
WO 2006113236	A3	20070531		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-671408P P 20050414

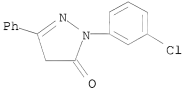
OTHER SOURCE(S): MARPAT 145:449207
GI



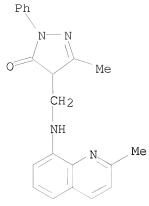
I

AB The invention discloses a method for treating an inflammatory disorder in a subject. The method involves administering to a subject an effective amount of a compound that modulates soluble adenylyl cyclase, thereby treating the inflammatory disorder in the subject. The invention also discloses a method of inhibiting respiratory burst in adherent neutrophils without inhibiting neutrophil degranulation in or bacterial killing by neutrophils. The method involves contacting adherent neutrophils with an effective amount of a compound that modulates soluble adenylyl cyclase. Compds.
of the invention include a number of benzimidazole derivs., e.g. I.

IT 108124-77-2
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical inhibitors of neutrophil activation through soluble adenyl cyclase-dependent pathway, and use for treatment of inflammatory disorders)
RN 108124-77-2 CAPLUS
CN 3H-Pyrazol-3-one, 2-(3-chlorophenyl)-2,4-dihydro-5-phenyl- (CA INDEX NAME)



IT 850306-02-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical inhibitors of neutrophil activation through soluble adenyl cyclase-dependent pathway, and use for treatment of inflammatory disorders)
RN 850306-02-4 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-4-[[(2-methyl-8-quinolinyl)amino]methyl]-2-phenyl- (CA INDEX NAME)

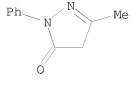


L9 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:967234 CAPLUS
DOCUMENT NUMBER: 146:514235
TITLE: Treatment With Edaravone Improves the Survival Rate in Renal Warm Ischemia-Reperfusion Injury Using Rat Model
AUTHOR(S): Matsuyama, M.; Hayama, T.; Funao, K.; Tsuchida, K.; Takemoto, Y.; Sugimura, K.; Kawahito, Y.; Sano, H.; Nakatani, T.; Yoshimura, R.
CORPORATE SOURCE: Department of Urology, Osaka City University Graduate School of Medicine, Osaka, Japan
SOURCE: Transplantation Proceedings (2006), 38(7), 2199-2200
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Renal ischemia-reperfusion (I/R) injury during renal transplantation is a significant cause of renal dysfunction. The pathol. role of free radicals in this process is a major concern. We investigated the effect of a free radical scavenger, edaravone (MCI-186), in renal I/R injury. Male Lewis rats (270 to 320 g) were used for the model. The right kidney was harvested and left renal artery and vein were clamped as laparotomy. The kidney was reperfused after 90 min of ischemia. Edaravone (10 mg/kg) was delivered i.v. before ischemia and after reperfusion to prevent the neutrophil activation. In the nontreatment I/R group, no rat survived beyond 4 days. However, in the edaravone I/R treatment group, one among five rats survived more than 7 days. These results suggested that treatment with edaravone ameliorated renal I/R injury, and that the agent has the potential to ameliorate preservation injury in renal transplantation.

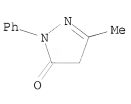
IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(edaravone improved survival and ameliorated renal warm ischemia-reperfusion injury in rat)

RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:309639 CAPLUS
DOCUMENT NUMBER: 145:499861
TITLE: 1,026 Experimental treatments in acute stroke
AUTHOR(S): O'Collins, Victoria E.; Macleod, Malcolm R.; Donnan, Geoffrey A.; Horky, Laura L.; van der Worp, Bart H.; Howells, David W.
CORPORATE SOURCE: Neuroscience Lab, Department of Medicine, Austin Health, University of Melbourne, Heidelberg, Australia
SOURCE: Annals of Neurology (2006), 59(3), 467-477
CODEN: ANNED3; ISSN: 0364-5134
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: Preclin. evaluation of neuroprotectants fostered high expectations of clin. efficacy. When not matched, the question arises whether expts. are poor indicators of clin. outcome or whether the best drugs were not taken forward to clin. trial. Therefore, we endeavored to contrast exptl. efficacy and scope of testing of drugs used clin. and those tested only exptl. Methods: We identified neuroprotectants and reports of exptl. efficacy via a systematic search. Controlled in vivo and in vitro expts. using functional or histol. end points were selected for anal. Relationships between outcome, drug mechanism, scope of testing, and clin. trial status were assessed statistically. Results: There was no evidence that drugs used clin. (114 drugs) were more effective exptl. than those tested only in animal models (912 drugs), for example, improvement in focal models averaged 31.3±16.7% vs. 24.4±32.9%, $p > 0.05$, resp. Scope of testing using Stroke Therapy Academic Industry Roundtable (STAIR) criteria was highly variable, and no relationship was found between mechanism and efficacy. Interpretation: The results question whether the most efficacious drugs are being selected for stroke clin. trials. This may partially explain the slow progress in developing treatments. Greater rigor in the conduct, reporting, and anal. of animal data will improve the transition of scientific advances from bench to bedside.
IT 89-25-8, MCI-186
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



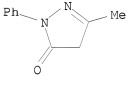
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:798963 CAPLUS
DOCUMENT NUMBER: 143:399723
TITLE: MCI-186 (edaravone), a free radical scavenger, attenuates hepatic warm ischemia-reperfusion injury in rats
AUTHOR(S): Suzuki, Fumitaka; Hashikura, Yasuhiko; Ise, Hirohiko; Ishida, Akiko; Nakayama, Jun; Takahashi, Masafumi; Miyagawa, Shin-ichi; Ikeda, Uichi
CORPORATE SOURCE: Department of Organ Regeneration, Shinshu University Graduate School of Medicine, Asahi, Matsumoto, Japan
SOURCE: Transplant International (2005), 18(7), 844-853 CODEN: TRINE5; ISSN: 0934-0874
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hepatic warm ischemia-reperfusion injury (IRI) during hepatectomy and liver transplantation is a major cause of liver dysfunction in which the pathol. role of free radicals is a major concern. To assess the effect of MCI-186 (edaravone) on hepatic IRI, male Wistar rats were subjected to partial hepatic ischemia for 60 min after pretreatment with vehicle (group C) or MCI-186 (group M), or after both MCI-186 pretreatment and addnl. administration of MCI-186 12 h after reperfusion (group MX). Groups M and MX showed significantly lower levels of serum alanine aminotransferase and hepatic lipid peroxidn. than group C, and also significantly lower expression levels of mRNA for cytokines, chemokines and intercellular adhesion mol.-1. There were fewer tissue monocytes and neutrophils in groups M and MX than in group C. These effects were more marked in group MX than in group M. Our findings suggest that treatment with MCI-186 attenuates hepatic IRI in this rat in vivo model.

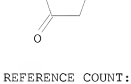
IT 89-25-8, MCI-186
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MCI-186 decreased serum alanine aminotransferase, hepatic lipid peroxidn., ICAM-1, TNF-α, IL-1, CINC-2, MIP-2, MCP-1, MIP-1α expression, showed few tissue monocyte, neutrophil in rat model of hepatic warm ischemia-reperfusion injury)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:422224 CAPLUS
DOCUMENT NUMBER: 143:241857
TITLE: A free radical scavenger, edaravone (MCI-186), diminishes intestinal neutrophil lipid peroxidation and bacterial translocation in a rat hemorrhagic shock model
AUTHOR(S): Mori, Tsuyoshi; Yamamoto, Hiroshi; Tabata, Takahisa; Shimizu, Tomoharu; Endo, Yoshihiro; Hanasawa, Kazuyoshi; Fujimiya, Mineko; Tani, Tohru
CORPORATE SOURCE: Department of Surgery and the Department of Anatomy,

Shiga University of Medical Science, Tsukinowa-cho, Otsu-shi Shiga, 520-2192, Japan
SOURCE: Critical Care Medicine (2005), 33(5), 1064-1069
CODEN: CCMDC7; ISSN: 0090-3493
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: To investigate the effects of edaravone, a novel free radical scavenger, on bacterial translocation induced by hemorrhagic shock. Design: Prospective, randomized, unblinded animal study. Setting: Surgical research labs. of Shiga University of Medical Science. Subjects: Male specific-pathogen-free Sprague-Dawley rats. Interventions: The rats were randomly divided into three groups: conventional saline treatment, edaravone treatment, and sham shock induction. The saline and edaravone groups were subjected to hemorrhagic shock (mean arterial pressure of 30 mm Hg, for 30 or 60 mins). Rats were killed 30 or 60 mins after shock induction. Mesenteric lymph nodes were cultured for determination of bacterial translocation. Systemic plasma silkworm larvae plasma test, which can detect peptidoglycan and β-glucan, and endotoxin tests were performed. Immunohistochem. for 4-hydroxy-2-nonenal (4-HNE) was used to assess lipid peroxidn. after shock. Measurements and main results: The incidence and magnitude of hemorrhagic-shock-induced bacterial translocation to mesenteric lymph nodes were reduced by edaravone. Hemorrhagic-shock-induced increase of plasma silkworm larvae plasma test was also reduced by edaravone. Immunohistochem. for 4-HNE showed many 4-HNE-pos. cells in the lamina propria of the ileum 60 mins after hemorrhagic shock. Double immunohistochem. revealed that many of these 4-HNE-pos. cells were also myeloperoxidase pos. Moreover, the percentage of double-labeled cells with 4-HNE and myeloperoxidase in myeloperoxidase-pos. cells was significantly lower in the edaravone group than in the saline group. Conclusions: The present findings suggest that lipid peroxidn. of intestinal neutrophils is involved in bacterial translocation during hemorrhagic shock and that edaravone is potentially useful in diminishing bacterial translocation after hemorrhagic shock.
IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(free radical scavenger edaravone reduced lipid peroxidn. of neutrophils and diminished bacterial translocation to lymph node at early phase in hemorrhagic shock rat model)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:405369 CAPLUS
DOCUMENT NUMBER: 142:463730
TITLE: Preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one choline salt

INVENTOR(S): Brook, Christopher S.; Ping, Li-Jen J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005041867	A2	20050512	WO 2004-US34944	20041021
WO 2005041867	A3	20051013		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004285462	A1	20050512	AU 2004-285462	20041021
CA 2543216	A1	20050512	CA 2004-2543216	20041021
EP 1684748	A2	20060802	EP 2004-796011	20041021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004015704	A	20061219	BR 2004-15704	20041021
CN 1897937	A	20070117	CN 2004-80038488	20041021
JP 2007509159	T	20070412	JP 2006-536801	20041021
IN 2006DN02031	A	20070622	IN 2006-DN2031	20060413
US 20070072922	A1	20070329	US 2006-576411	20060420
MX 2006004483	A	20060620	MX 2006-4483	20060421
KR 2006095761	A	20060901	KR 2006-707688	20060421
NO 2006002111	A	20060718	NO 2006-2111	20060511
PRIORITY APPLN. INFO.:			US 2003-513481P P	20031022
			WO 2004-US34944 W	20041021

OTHER SOURCE(S): CASREACT 142:463730
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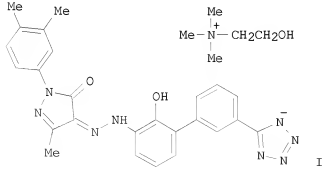


I

AB An improved thrombopoietin mimetic, the choline salt of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-

hydrazono]-5-methyl-2,4-dihydropyrazol-3-one (I), is prepared by treating 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one with choline hydroxide. The compound I is useful as an agonist of thrombopoietin receptor in enhancing platelet production, particularly in the treatment of thrombocytopenia. A tablet and injectable parenteral composition containing I are described.

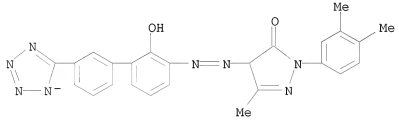
IT 851606-62-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

RN 851606-62-7 CAPLUS

CN Ethanaminium, 2-hydroxy-N,N,N-trimethyl-, salt with 2-(3,4-dimethylphenyl)-2,4-dihydro-4-[2-[2-hydroxy-3'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]diazenyl]-5-methyl-3H-pyrazol-3-one (1:1) (CA INDEX NAME)

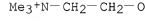
CM 1

CRN 851606-61-6
CMF C25 H21 N8 O2



CM 2

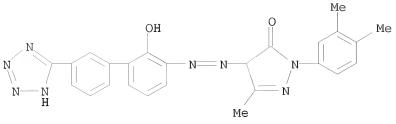
CRN 62-49-7
CMF C5 H14 N O



IT 376592-42-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

RN 376592-42-6 CAPLUS

CN 3H-Pyrazol-3-one, 2-(3,4-dimethylphenyl)-2,4-dihydro-4-[2-[2-hydroxy-3'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]diazenyl]-5-methyl- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:369234 CAPLUS
DOCUMENT NUMBER: 142:404249
TITLE: Treating an inflammatory disorder or inhibiting respiratory burst in adherent neutrophils with chemical inhibitors of neutrophil activation
INVENTOR(S): Han, Hyunsil; Lin, Gang; Nathan, Carl F.
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037213	A2	20050428	WO 2004-US33914	20041014
WO 2005037213	A3	20060713		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20070021448	A1	20070125	US 2006-575683	20060831
PRIORITY APPLN. INFO.:			US 2003-510843P P	20031014
			WO 2004-US33914 W	20041014

OTHER SOURCE(S): MARPAT 142:404249
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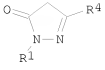
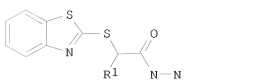
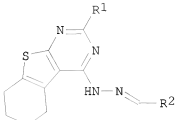


I

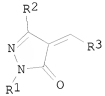


II



III

IV



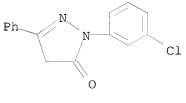
V

AB The present invention relates to a method of treating an inflammatory disorder in a subject with an effective amount of compound having the general formula I-V as described in the present application, under conditions effective to treat the inflammatory disorder. The present invention also relates to a method of inhibiting respiratory burst in neutrophils without inhibiting degranulation in or bacterial killing by the neutrophils by contacting neutrophils with the compds. described above. A combinatorial library of 15,000 compds. was screened for specific inhibitors of TNF- and PMA-triggered H2O2 release by primary human neutrophils. A small number of compds. were identified as capable of inhibiting TNF-triggered respiratory burst, as measured by H2O2 release, without inhibiting PMA-triggered respiratory burst.

IT 108124-77-2 850306-02-4
RL: BSU (Biological study, unclassified); CST (Combinatorial study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); USES (Uses)
(treatment of inflammatory disorder or inhibition of respiratory burst in adherent neutrophils with chemical inhibitors of neutrophil activation)

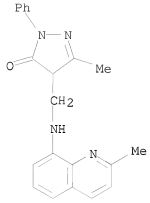
RN 108124-77-2 CAPLUS

CN 3H-Pyrazol-3-one, 2-(3-chlorophenyl)-2,4-dihydro-5-phenyl- (CA INDEX NAME)



RN 850306-02-4 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-4-[[(2-methyl-8-quinolinyl)amino]methyl]-2-phenyl- (CA INDEX NAME)

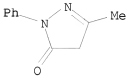


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:312406 CAPLUS
DOCUMENT NUMBER: 142:441519
TITLE: Effects of edaravone on human neutrophil function
AUTHOR(S): Mikawa, K.; Akamatsu, H.; Nishina, K.; Obara, H.; Niwa, Y.
CORPORATE SOURCE: Department of Anesthesia & Perioperative Medicine, Faculty of Medical Sciences, Kobe University Graduate School of Medicine, Kobe, Japan
SOURCE: Acta Anaesthesiologica Scandinavica (2005), 49(3), 385-389
CODEN: AANEAB; ISSN: 0001-5172
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Neutrophils play a crucial role in the antibacterial host defense system. Edaravone is used in critically ill patients who are often immuno-compromised secondary to concomitant disease or immunosuppressive therapy. The aim of the current study was to assess the effect of edaravone, a novel free-radical scavenger, on several aspects of human neutrophil function using an in vitro system. Methods: Chemotaxis, phagocytosis, reactive oxygen species (ROS) production by neutrophil (cellular) and xanthine-xanthine oxidase (acellular) systems, and intracellular calcium ion levels ([Ca2+]i) were measured in the absence and in the presence (at a clin. relevant concentration, and 0.1-fold, and 10-fold this concentration) of edaravone. Results: The clin. relevant concentration of edaravone did not inhibit chemotaxis, phagocytosis, or superoxide production of neutrophils. Even at its ordinary clin. plasma concentration, the drug inhibited hydrogen peroxide (H2O2) and hydroxyl radical (OH·) generation in the cellular (neutrophil) as well as in the cell-free (xanthine-xanthine oxidase) system ($P < 0.05$). Edaravone did not affect elevation of [Ca2+]i in neutrophils stimulated by a chemotactic factor. Conclusions: These findings suggest that edaravone quenched H2O2, and OH· generated rather than impaired the ability of neutrophils to produce the ROS. However, further studies using in vivo systems are required to elucidate the effects of edaravone on neutrophil function in clin. settings.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(edaravone did not effect chemotaxis, phagocytosis, superoxide production and intracellular resting calcium in human neutrophils but inhibited hydrogen peroxide and hydroxyl radical generation in xanthine-xanthine oxidase cell free system)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:260029 CAPLUS
DOCUMENT NUMBER: 142:316706
TITLE: Preparation of 2-pyridone derivatives as neutrophil elastase inhibitors and their use for treating inflammation
INVENTOR(S): Hansen, Peter; Lawitz, Karolina; Loenn, Hans; Nikitidis, Antonios
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005026124	A1	20050324	WO 2004-SE1336	20040915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004272485	A1	20050324	AU 2004-272485	20040915
AU 2004272485	B2	20080313		
CA 2538410	A1	20050324	CA 2004-2538410	20040915
EP 1663974	A1	20060607	EP 2004-775439	20040915
EP 1663974	B1	20090114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1856467	A	20061101	CN 2004-80027517	20040915
CN 100439339	C	20081203		
BR 2004014570	A	20061107	BR 2004-14570	20040915

JP 2007505902	T	20070315	JP 2006-526856		20040915
AT 420861	T	20090115	AT 2004-775439		20040915
RU 2348617	C2	20090310	RU 2006-112427		20040915
MX 2006002723	A	20060606	MX 2006-2723		20060309
US 20070043036	A1	20070222	US 2006-572640		20060317
IN 2006DN02073	A	20070713	IN 2006-DN2073		20060417
NO 2006001700	A	20060418	NO 2006-1700		20060418
PRIORITY APPLN. INFO.:			SE 2003-2487	A	20030918
			WO 2004-GB1336	W	20040915
			WO 2004-SE1336	W	20040915

OTHER SOURCE(S): CASREACT 142:316706; MARPAT 142:316706

GI

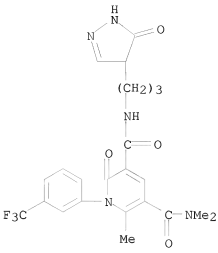
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein Y = CH, CF, N; R1 = H, alkyl; R2 = CN, NO2, OH, (un)substituted alk(en/yn)yl, ; G1 = Ph, 5- or 6-membered heteroaryl containing 1 to 3 heteroatoms; each R5 = independently H, halo, CN, alkoxy, NO2, etc.; n = 1-3; R4 = H, (un)substituted alkyl; L = a bond, O, NH, N-alkyl, (un)substituted alkyl; G2 = (un)substituted monocyclyl, bicyclyl; and their optical isomers, racemates, tautomers, and pharmaceutically acceptable salts] were prepared as human neutrophil elastase (HNE) inhibitors for treating inflammation. Thus, acylation of 4-methylsulfonylbenzylamine•HCl with 6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2-dihydropyridine-3-carboxylic acid (preparation given), iodination, and cyanation of the iodide with CuCN gave pyridone II. Selected I gave IC50 values for inhibition of HNE activity of less than 30 μM.

IT 848184-32-7P, N5,N5,6-Trimethyl-2-oxo-N3-[3-(5-oxo-4,5-dihydro-1H-pyrazol-4-yl)propyl]-1-[3-(trifluoromethyl)phenyl]-1,2-dihydropyridine-3,5-dicarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 2-pyridones as human neutrophil elastase inhibitors and their use for treating inflammation)

RN 848184-32-7 CAPLUS

CN 3,5-Pyridinedicarboxamide, N3-[3-(4,5-dihydro-5-oxo-1H-pyrazol-4-yl)propyl]-1,2-dihydro-N5,N5,6-trimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:260028 CAPLUS
DOCUMENT NUMBER: 142:316705
TITLE: Preparation of 2-pyridone derivatives as neutrophil elastase inhibitors and their use for treating inflammation
INVENTOR(S): Andersson, Marjana; Hansen, Peter; Loenn, Hans; Nikitidis, Antonios; Sjoelin, Petter
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005026123	A1	20050324	WO 2004-SE1335	20040915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004272484	A1	20050324	AU 2004-272484	20040915
AU 2004272484	B2	20080313		
CA 2538405	A1	20050324	CA 2004-2538405	20040915
EP 1663973	A1	20060607	EP 2004-775438	20040915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004014548	A	20061107	BR 2004-14548	20040915
CN 1882542	A	20061220	CN 2004-80033847	20040915
JP 2007505901	T	20070315	JP 2006-526855	20040915

RU 2353616	C2	20090427	RU 2006-112428		20040915
MX 2006002724	A	20060606	MX 2006-2724		20060309
KR 2006087569	A	20060802	KR 2006-705456		20060317
NO 2006001660	A	20060411	NO 2006-1660		20060411
IN 2006DN02107	A	20070713	IN 2006-DN2107		20060418
US 20070203129	A1	20070830	US 2007-572706		20070108
PRIORITY APPLN. INFO.:			SE 2003-2486	A	20030918
			WO 2004-SE1335	W	20040915

OTHER SOURCE(S): CASREACT 142:316705; MARPAT 142:316705

GI

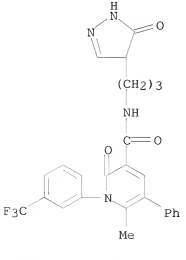
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein Y = CH, CF, N; R1 = H, alkyl; R2 = (un)substituted Ph, 5- or 6-membered heteroaryl containing 1 to 4 heteroatoms; G1 = Ph, 5- or 6-membered heteroaryl containing 1 to 3 heteroatoms; each R5 = independently H, halo, CN, alkoxy, NO2, etc.; n = 1-3; R4 = H, (un)substituted alkyl; L = a bond, O, SO, SO2, S, NH, etc.; G2 = (un)substituted monocyclyl, bicyclyl; and their optical isomers, racemates, tautomers, and pharmaceutically acceptable salts] were prepared as human neutrophil elastase (HNE) inhibitors for treating inflammation. Thus, acylation of 4-methylsulfonylbenzylamine•HCl with 6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2-dihydropyridine-3-carboxylic acid (preparation given), iodination, and Pd-cross coupling of the iodide with phenylboronic acid gave pyridone II. Selected I gave IC50 values for inhibition of HNE activity of less than 30 μM.

IT 848141-01-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 2-pyridones as human neutrophil elastase inhibitors and their use for treating inflammation)

RN 848141-01-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[3-(4,5-dihydro-5-oxo-1H-pyrazol-4-yl)propyl]-1,2-dihydro-6-methyl-2-oxo-5-phenyl-1-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



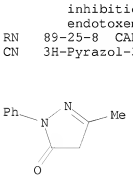
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:4469 CAPLUS
DOCUMENT NUMBER: 142:329460
TITLE: Free radical scavenger (edaravone) prevents endotoxin-induced liver injury after partial hepatectomy in rats
AUTHOR(S): Tsuji, Katsushige; Kwon, A-Hon; Yoshida, Hideyuki; Qiu, Zeyu; Kaibori, Masaki; Okumura, Tadayoshi; Kamiyama, Yasuo
CORPORATE SOURCE: Department of Surgery, Kansai Medical University, 10-15 Fumizono, Moriguchi, Osaka, 570-8507, Japan
SOURCE: Journal of Hepatology (2005), 42(1), 94-101
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Infection after major surgery, such as massive hepatectomy, induces liver dysfunction, occasionally leading to multiple organ failure and death. We demonstrated the anti-inflammatory effects and functional mechanisms of 3-methyl-1-phenyl-2-pyrazolin-5-one (edaravone), a newly synthesized free radical scavenger, on an exptl. model of endotoxemia after partial hepatectomy in rats. Rats were treated with lipopolysaccharide (LPS) 48 h after 70% hepatectomy. Edaravone was administered i.v. before LPS-treatment. Edaravone markedly improved the survival rate of LPS-treated rats after hepatectomy and inhibited increases in serum levels of AST and LDH. Histopathol. anal. demonstrated that edaravone prevented inflammatory changes in the liver, kidney and spleen. Edaravone inhibited the formation of one of the markers of oxidative damage, malondialdehyde. Increases in inflammatory cytokines and cytokine-induced neutrophil chemoattractant (CINC) in serum and liver tissue were inhibited in the edaravone-treated group. An electrophoretic mobility shift assay revealed that edaravone inhibited the activation of the transcription factor, nuclear factor-kappa B (NF-κB). Edaravone also reduced the induction of inducible nitric oxide synthase (iNOS). Edaravone prevents endotoxin-induced liver injury after partial hepatectomy not only by attenuating oxidative damage, but also by reducing the production of inflammatory cytokines, CINC and iNOS, in part through the inhibition of NF-κB activation.

IT 89-25-8, Edaravone
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(free radical scavenger edaravone prevented liver injury by attenuating oxidative damage, reducing inflammatory cytokines, CINC, iNOS, inhibition of NF-κB activation in rat model of LPS-induced endotoxemia after partial hepatectomy)

RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

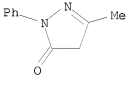
L9 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:3433 CAPLUS
DOCUMENT NUMBER: 142:190815
TITLE: Edaravone protects against lung injury induced by intestinal ischemia/reperfusion in rat
AUTHOR(S): Ito, Koji; Ozasa, Hisashi; Horikawa, Saburo
CORPORATE SOURCE: Department of Pathological Biochemistry, Medical Research Institute, Tokyo Medical and Dental University, Chiyoda-ku, Tokyo, 101-0062, Japan
SOURCE: Free Radical Biology & Medicine (2005), 38(3), 369-374
CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intestinal ischemia/reperfusion (I/R) is a critical and triggering event in the development of distal organ dysfunction, frequently involving the lungs. Respiratory failure is a common cause of death and complications after intestinal I/R. In this study the authors investigated the effects of edaravone (3-methyl-1-phenyl-2-pyrazoline-5-one) on the prevention of lung injury induced by intestinal I/R in rats. Edaravone was used for protection against I/R injury in patients with cerebral infarction. When rats were subjected to 180 min of intestinal ischemia, a high incidence of mortality was observed within 24 h. In this situation, i.v. administration of edaravone just before the start of reperfusion reduced the mortality in a dose-dependent manner. To examine the efficacy of edaravone on the lung injury induced by intestinal I/R in more detail, the authors performed 120 min of intestinal ischemia followed by 120 min of reperfusion. Edaravone treatment decreased the neutrophil infiltration, the lipid membrane peroxidn., and the expression of proinflammatory cytokine interleukin-6 mRNA in the lungs after intestinal I/R compared to the I/R-treated rat lungs without edaravone treatment. Histopathol. anal. also indicated the effectiveness of edaravone. In conclusion, edaravone ameliorated the lung injury induced by intestinal I/R, resulting in a reduction in mortality.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(edaravone protects against lung injury induced by intestinal ischemia/reperfusion in rat)

RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

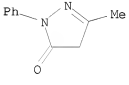
L9 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:540337 CAPLUS
DOCUMENT NUMBER: 142:49133
TITLE: Antioxidant effect of MCI-186, a new Free-Radical scavenger, on ischemia-reperfusion injury in a rat hindlimb amputation model
AUTHOR(S): Irie, H.; Kato, T.; Ikebe, K.; Tsuchida, T.; Oniki, Y.; Takagi, K.
CORPORATE SOURCE: Department of Orthopedic Surgery, Kumamoto University

School of Medicine, Kumamoto, 861-1102, Japan
SOURCE: Journal of Surgical Research (2004), 120(2), 312-319
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: A newly synthesized free-radical scavenger, MCI-186 (3-methyl-1-phenyl-2-pyrazolin-5-1), was recently approved in Japan for treating acute brain infarction. The purpose of this study was to investigate whether or not MCI-186 is effective in reducing ischemia-reperfusion injury in the extremities. Materials and Methods: Warm ischemia was sustained for 4 h. The animals were divided into 4 groups: (1) sham group, (2) control group (saline injection), (3) MCI group (MCI-186 injection), and (4) EPC group (EPC-K1 [(L-ascorbic acid 2-[3,4-dihydro-2, 5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-yl hydrogen phosphate] potassium salt], a hydroxyl-radical scavenger, injection). Wet and dry (W/D) wts. of the gastrocnemius and tibialis anterior muscles, muscle contractile function, and serum levels of creatine phosphokinase (CPK), lactate dehydrogenase (LDH), glutamic oxaloacetic transminase (GOT), and mitochondrial glutamic oxaloacetic transminase (GOT-m) were measured after 24 h of reperfusion. The cytotoxic aldehydes malondialdehyde and 4-hydroxy-2-nonenal as indexes of lipid peroxidn. (LPO), and neutrophil-specific enzyme myeloperoxidase (MPO) as an index of neutrophil infiltration, were measured in the gastrocnemius muscle. Results: Contractile functions in the MCI and EPC groups were significantly better than in the control group. In the tibialis anterior muscle, the contractile function was better in the MCI group than in the EPC group. W/D ratios and serum levels of CPK, LDH, GOT, and GOT-m were lower in the sham and MCI groups than in the control group. Levels of LPO and MPO activity were significantly lower in the MCI and EPC groups than in the control group. Histol. findings demonstrated that inflammatory tissue reactions rarely occurred in the MCI group. Conclusion: MCI-186 is effective in preventing ischemia-reperfusion injury in extremities. MCI-186 seems to have promise as a therapeutic agent, because it prevents ischemia-reperfusion injury even in the tibialis anterior muscle, which contains fast-twitch glycolytic fibers, known to be very susceptible to ischemic insult.

IT 89-25-8, MCI-186
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MCI-186 prevented ischemia-reperfusion injury in gastrocnemius, tibialis muscles by improving muscle contractile function, decreasing LPO, MPO, serum CPK, GOT, LDH, GOT-m activity and water content than EPC in rat hindlimb amputation model)

RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 28 CAPLUS
ACCESSION NUMBER: 2004:428910 CAPLUS
DOCUMENT NUMBER: 141:7027

TITLE: Preparation of 2-pyridone derivatives as inhibitors of neutrophile elastase

INVENTOR(S): Bladh, Hakan; Klingstedt, Tomas; Larsson, Joakim; Lawitz, Karolina; Lepistoe, Matti; Loenn, Hans; Nikitidis, Grigorios

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043924	A1	20040527	WO 2003-SE1739	20031111
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2504766	A1	20040527	CA 2003-2504766	20031111
AU 2003276802	A1	20040603	AU 2003-276802	20031111
AU 2003276802	B2	20070308		
EP 1562902	A1	20050817	EP 2003-811770	20031111
EP 1562902	B1	20060503		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016081	A	20050927	BR 2003-16081	20031111
CN 1711243	A	20051221	CN 2003-80103085	20031111
JP 2006513261	T	20060420	JP 2005-506687	20031111
AT 325096	T	20060615	AT 2003-811770	20031111
ES 2262029	T3	20061116	ES 2003-811770	20031111
NZ 539787	A	20061130	NZ 2003-539787	20031111
RU 2328486	C2	20080710	RU 2005-113168	20031111
IN 2005DN01638	A	20070119	IN 2005-DN1638	20050421
MX 2005004818	A	20050722	MX 2005-4818	20050504
ZA 2005003710	A	20061129	ZA 2005-3710	20050509
US 20060035938	A1	20060216	US 2005-534720	20050512
HK 1079200	A1	20061006	HK 2005-111156	20051206

PRIORITY APPLN. INFO.:			
SE 2002-3348	A	20021112	
SE 2003-388	A	20030212	
SE 2003-2120	A	20030722	
WO 2003-SE1739	W	20031111	

OTHER SOURCE(S): MARPAT 141:7027

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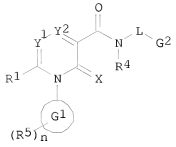

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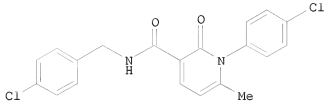


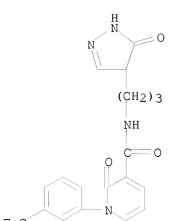
II

AB Title compds. I [X = O, S; Y1 = N, CR2 and when R1 = OH, Y1 may also, in the tautomeric form, represent NR6; Y2 = CR3 and when Y1 = CR2, then Y2 may also represent N; R1 = H, alkyl; R2 = H, halo, alkyl; R3 = H, F; G1 = Ph, 5-6 membered heterocycle, etc.; R5 = H, halo, alkyl, etc.; n = 1-3; R4, R6 = H, alkyl, etc.; L = O, amino, alkyl, etc.; G2 = Ph, phenoxy, etc.] are prepared For instance, Et 3-[(4-chlorophenyl)amino]-3-oxopropanoate is reacted with 4-methoxy-3-buten-2-one (EtOH, NaOMe, reflux, 5 h) to give Et 1-(4-chlorophenyl)-6-methyl-2-oxo-1,2-dihydropyridine-3-carboxylate. This intermediate is saponified and coupled to 4-chlorobenzylamine (NMP, HBTu, HOBt, DIEA) to give II. Selected compds. have IC50 < 30 μM for human neutrophil elastase. I are useful in the treatment of inflammatory disorders.

IT 694482-31-0P, 6-Methyl-2-oxo-N-[3-(5-oxo-4,5-dihydro-1H-pyrazol-4-yl)propyl]-1-[3-(trifluoromethyl)phenyl]-1,2-dihydropyridine-3-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-pyridone derivs. as inhibitors of neutrophile elastase)

RN 694482-31-0 CAPLUS

CN 3-Pyridinecarboxamide, N-[3-(4,5-dihydro-5-oxo-1H-pyrazol-4-yl)propyl]-1,2-dihydro-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:72694 CAPLUS

DOCUMENT NUMBER: 141:17516

TITLE: Edaravone, a newly developed radical scavenger, protects against ischemia-reperfusion injury of the small intestine in rats

AUTHOR(S): Tomatsuri, Naoya; Yoshida, Norimasa; Takagi, Tomohisa; Katada, Kazuhiro; Isozaki, Yutaka; Imamoto, Eiko; Uchiyama, Kazuhiko; Kokura, Satoshi; Ichikawa, Hiroshi; Naito, Yuji; Okanoue, Takeshi; Yoshikawa, Toshikazu

CORPORATE SOURCE: Departments of Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, 602-8566, Japan

SOURCE: International Journal of Molecular Medicine (2004), 13(1), 105-109
CODEN: IJMMFG; ISSN: 1107-3756

PUBLISHER: International Journal of Molecular Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English

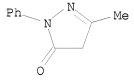
AB Although edaravone (3-methyl-1-phenyl-pyrazolin-5-one), a newly developed radical scavenging agent, has been widely used for protection against ischemia-reperfusion (I-R) injury in patients with cerebral infarction, its effects on gastrointestinal I-R injury have not been evaluated. In the present study, we examined the effects of edaravone on exptl. intestinal I-R damage in rats. In male Wistar rats with and without edaravone treatment, intestinal damage was induced by clamping the superior mesenteric artery for 30 min, followed by reperfusion. Edaravone was administered via i.v. infusion at 5 min before reperfusion was achieved by removal of the clamp. The rats were sacrificed after 60 min of reperfusion. Luminal protein and Hb concns. were measured as an index of mucosal injury and histol. examination of hematoxylin and eosin-stained sections was performed. Thiobarbituric acid (TBA)-reactive substances and tissue-associated myeloperoxidase (MPO) activity were measured in the mucosa as indicators of lipid peroxidn. and neutrophil infiltration, resp. The mucosal concentration of cytokine-induced neutrophil chemoattractant (CINC)-1 (a member of the IL-8 family) was determined by ELISA. Addnl., CINC-1 mRNA (mRNA) was measured by the reverse-transcription polymerase chain reaction (RT-PCR). As a result, the levels of luminal

protein and Hb, TBA-reactive substances, and MPO activity were all increased significantly by I-R injury, and these increases were significantly inhibited by treatment with edaravone. Multiple erosions and bleeding were observed macroscopically after the small intestine was exposed to I-R injury, and these changes were inhibited by administration of edaravone. Microscopic I-R damage was also reduced by treatment with edaravone. CINC-1 protein and CINC-1 mRNA were both increased by I-R injury, while edaravone markedly reduced the levels of both protein and mRNA. In summary, these results suggest that edaravone can protect the small intestine against I-R injury by scavenging oxygen-derived free radicals.

IT 89-25-8, Edaravone
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of radical scavenger edaravone on ischemia-reperfusion injury of small intestine)

RN 89-25-8 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:353018 CAPLUS

DOCUMENT NUMBER: 129:38385

ORIGINAL REFERENCE NO.: 129:8013a,8016a

TITLE: Photographic color couplers used as cytochemical contrast markers for detecting the presence of peroxidatively active species

INVENTOR(S): Saunders, Alexander Michael; Lin, Emily; Godecke, Cameron

PATENT ASSIGNEE(S): Applied Imaging Corp., USA

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

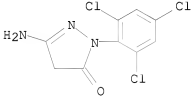
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822822	A1	19980528	WO 1997-US21515	19971121
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9854556	A	19980610	AU 1998-54556	19971121
PRIORITY APPLN. INFO.:			US 1996-754723	A 19961121
			WO 1997-US21515	W 19971121

AB Novel methods of detecting peroxidatively active species in biol. samples, such as blood and tissue cells, are disclosed. Peroxidativelyactive species are peroxidase enzyme, myoglobins or Hbs. The methods comprise using combinations of peroxidase substrates and photog. color couplers, e.g. a yellow, magenta or cyan coupler. The biol. sample is contacted with a reaction mixture comprising peroxidase substrate, peroxide, and the photog. color coupler. The formed fluorescent product can be detected by flow cytometry or microscopy. In a version of the method at least two different peroxidatively active species in a single biol. sample are determined simultaneously. An other version enables the detection of a cell carrying both peroxidatively active species and non-peroxidative enzyme. The invention also includes a test kit comprising the photog. color coupler(s), a peroxidase substrate, peroxidase enzyme or a non-peroxidase enzyme, and selective peroxidase inhibitor(s).

IT 2'241-31-2
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (photog. color couplers used as cytochem. contrast markers for detecting presence of peroxidatively active species)

RN 2'241-31-2 CAPLUS

CN 3H-Pyrazol-3-one, 5-amino-2,4-dihydro-2-(2,4,6-trichlorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1996:248056 CAPLUS

DOCUMENT NUMBER: 124:283'04

ORIGINAL REFERENCE NO.: 124:52419a,52422a

TITLE: A method for classifying and counting leukocytes

INVENTOR(S): Takarada, Kaoru; Kouzuki, Chihiro; Hyousa, Yoshihiro; Sakata, Takashi; Akai, Yasumasa

PATENT ASSIGNEE(S): Toa Medical Electronics Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 695936	A2	19960207	EP 1995-610036	19950616
EP 695936	A3	19970813		
EP 695936	B1	20020904		
R: DE, FR, GB, IT				
JP 08043381	A	19960216	JP 1994-182633	19940803
JP 3355038	B2	20021209		
US 5677183	A	19971014	US 1995-464056	19950605
CA 2151667	A1	19960204	CA 1995-2151667	19950613
CN 1126836	A	19960717	CN 1995-115317	19950802
CN 1113241	C	20030702		

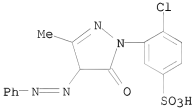
PRIORITY APPLN. INFO.: JP 1994-182633 A 19940803
OTHER SOURCE(S): MARPAT 124:283704

AB A method for classifying and counting leukocytes is disclosed that includes the steps of (1) adding a first reagent used for classifying leukocytes into 4 groups that comprises (a) at least one ionic surfactant in a sufficient amount to lyse erythrocytes and to damage a part of cell membrane of leukocytes, (b) at least one organic compound having an anionic group in a sufficient amount to bond with a cationic component present in leukocytes to give morphol. differences between leukocytes, (c) a nonionic surfactant, and (d) a buffer for adjusting pH, to a part of a blood sample to determine information on the cell size and morphol. features to classify leukocytes into 4 groups consisting of 3 groups corresponding to lymphocytes, mononuclear cells and eosinophils and 1 group corresponding to neutrophils and basophils; (2) adding a second reagent used for measuring basophils to another part of the blood sample to determine information on at least the cell size to classify basophils, and (3) classifying leukocytes based on the information obtained in steps (1) and (2) and counting with a simple photodiode-containing sensor.

IT 6359-90-6, c.i. Acid yellow 34
RL: BUU (Biological use, unclassified); NUU (Other use, unclassified); BIOL (Biological study); USES (Uses)
(method and apparatus for classifying and counting leukocytes)

RN 6359-90-6 CAPLUS

CN Benzenesulfonic acid, 4-chloro-3-[4,5-dihydro-3-methyl-5-oxo-4-(2-phenyldiazenyl)-1H-pyrazol-1-yl]-, sodium salt (1:1) (CA INDEX NAME)



● Na

L9 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:55133 CAPLUS
DOCUMENT NUMBER: 116:55133
ORIGINAL REFERENCE NO.: 116:9447a,9450a
TITLE: Reagent for measurement of leukocytes and hemoglobin in blood
INVENTOR(S): Sakata, Takashi
PATENT ASSIGNEE(S): Toa Medical Electronics Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 444241	A1	19910904	EP 1990-120293	19901023
EP 444241	B1	19950111		
R: DE, FR, GB, IT, NL				

JP 03252557	A	19911111	JP 1990-50813	19900301
JP 2891302	B2	19990517		
JP 04013969	A	19920117	JP 1990-116658	19900502
JP 2897781	B2	19990531		
US 5242832	A	19930907	US 1990-596205	19901010
CA 2027451	A1	19910902	CA 1990-2027451	19901012
CA 2027451	C	20020723		

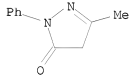
PRIORITY APPLN. INFO.: JP 1990-50813 A 19900301
JP 1990-116658 A 19900502

OTHER SOURCE(S): MARPAT 116:55133

AB The title cyanide-free stable reagent contains: (a) ≥1 cationic surfactant quaternary ammonium or pyridinium salts; (b) ≥1 cationic, nonionic, or amphoteric surfactant; and (c) ≥1 Hb stabilizer, e.g. Tiron. A preferred reagent contained lauryltrimethylammonium Cl 1.50, cetyltrimethylammonium Cl 0.40 g, phosphate buffer 1/25 M (pH 6.0), Tiron 300 mg, H2O 1 L, and NaCl.

IT 89-25-8, 3-Methyl-1-phenyl-5-pyrazolone 876-92-6D, derivs.
RL: ANST (Analytical study)
(as Hb stabilizer in reagent for Hb determination and counting of leukocytes)

RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



RN 876-92-6 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-phenyl- (CA INDEX NAME)

L9 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:464010 CAPLUS
DOCUMENT NUMBER: 115:64010
ORIGINAL REFERENCE NO.: 115:10823a,10826a
TITLE: The interaction of 3,5-pyrazolidinedione drugs with receptors for f-Met-Leu-Phe on human neutrophil leukocytes: a study of the structure-activity relationship
AUTHOR(S): Levesque, Luc; Gaudreault, Rene C.; Marceau, Francois
CORPORATE SOURCE: Fac. Med., Univ. Laval, Quebec, QC, G1K 7P4, Can.
SOURCE: Canadian Journal of Physiology and Pharmacology (1991), 69(3), 419-25
CODEN: CJPPA3; ISSN: 0008-4212
DOCUMENT TYPE: Journal
LANGUAGE: English

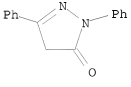
AB The 3,5-pyrazolidinedione (3,5-P) drugs, phenylbutazone and

sulfinpyrazone, have been reported to bind to receptors for the chemotactic peptide f-Met-Leu-Phe, and to behave as functional antagonists of f-Met-Leu-Phe in human and rabbit neutrophils. To explore the structure-activity relationship of this family of drugs for f-Met-Leu-Phe receptor binding, 36 drugs with the 3,5-P structure, a structure related to antipyrine, or an unrelated structure were tested as competitors for the binding of f-Met-Leu-Phe-Lys-fluorescein isothiocyanate on human neutrophils by flow cytometric anal. Only drugs possessing the 3,5-P ring were significant competitors. The five most potent 3,5-Ps behaved as selective antagonists of f-Met-Leu-Phe-induced superoxide anion release by neutrophils. The potency was not correlated to the pKa or to their capacity to inhibit prostaglandin E2 released from culture fibroblasts but instead appeared to be correlated to their apparent octanol-buffer partition coeffs. The most potent f-Met-Leu-Phe antagonist identified, 1,2-diphenyl-4-(3-(1-naphthyl)propyl)-3,5-pyrazolidinedione (DPN), may also possess an improved pharmacodynamic specificity compared with phenylbutazone and sulfinpyrazone, as it was less potent than phenylbutazone in the inhibition of prostaglandin synthesis and it was not cytotoxic. DPN may be a prototype for a valuable new class of anti-inflammatory drugs.

IT 4845-49-2
RL: BIOL (Biological study)
(chemotactic peptide receptor-binding activity of, in human neutrophils, structure in relation to)

RN 4845-49-2 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-2,5-diphenyl- (CA INDEX NAME)

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L6               STRUCTURE UPLOADED
L7         24092 S L6 FULL

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structure-building or screen commands and text search terms.  L#s
created via the STRUCTURE or SCREEN commands must be searched in the
structures files separately from text terms or profiles.  The L#
answer sets from structure searches can be used in crossover searches
and can be combined with text terms.

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CA SUBSCRIBER PRICE                                 0.00     -24.60

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FILE LAST UPDATED: 12 May 2009  (20090512/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Feb 2009

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

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L10       16286 L8 AND PY<2004

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L11          88 L10 AND INFLAMMATION

=> s l11 and treatment
       2592886 TREATMENT
L12          30 L11 AND TREATMENT

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L12  ANSWER 1 OF 30  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2005:497502  CAPLUS
DOCUMENT NUMBER:          143:53440
TITLE:                    Substituted benzoimidazole compounds as transcription
                          factor-modulating compounds useful as anti-infectives
INVENTOR(S):              Levy, Stuart B.; Alekshun, Michael N.; Podlogar, Brent
                          L.; Ohemeng, Kwasi; Verma, Atul K.; Warchol, Tadeusz;
                          Bhatia, Beena; Bowser, Todd; Grier, Mark
PATENT ASSIGNEE(S):       Paratek Pharmaceuticals, Inc., USA
SOURCE:                   U.S. Pat. Appl. Publ., 463 pp., Cont.-in-part of U.S.
                          Ser. No. 139,591.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   4
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
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     US 20050124678         A1    20050609    US 2003-700661           20031103
     US 7405235             B2    20080729
     CA 2445515             A1    20021104    CA 2002-2445515          20020506 <--
     AU 2002367953          A1    20040106    AU 2002-367953           20020506
     AU 2002367953          B2    20080717
     EP 1524974             A2    20050427    EP 2002-807554           20020506
          R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005519998          T     20050707    JP 2004-515557           20020506
     US 20030229065         A1    20031211    US 2002-139591           20020814 <--
     US 20040106553         A1    20040603    US 2003-602562           20030624
     AU 2008203017          A1    20080731    AU 2008-203017           20080708
PRIORITY APPLN. INFO.:                         US 2001-288660P      P   20010504
                                               US 2002-139591       A2  20020814
                                               US 2002-423319P      P   20021101
                                               US 2002-425916P      P   20021113
                                               AU 2002-367953       A3  20020506
                                               WO 2002-US14255      W   20020506
                                               US 2002-391345P      P   20020624
                                               US 2002-421218P      P   20021025
                                               US 2002-429142P      P   20021126
                                               US 2003-458935P      P   20030331
OTHER SOURCE(S):          MARPAT 143:53440
AB   Substituted benzoimidazole compds. useful as anti-infectives that decrease
     resistance, virulence, or growth of microbes are provided.  Methods of
     making and using substituted benzoimidazole compds., as well as
     pharmaceutical prepns. thereof, in, e.g., reducing antibiotic resistance
     and inhibiting biofilms.  The present invention identifies microbial
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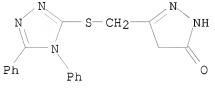
transcription factors, especially transcription factors of the AraC-XylS family,
as virulence factors in microbes and shows that inhibition of these factors reduces the virulence of microbial cells. Because these transcription factors control virulence, rather than essential cellular processes, the development of resistance is much less likely.

IT 305337-60-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted benzoimidazole compds. as transcription factor-modulating compds. useful as anti-infectives)

RN 305337-60-4 CAPLUS

CN 3H-Pyrazol-3-one, 5-[[(4,5-diphenyl-4H-1,2,4-triazol-3-yl)thio]methyl]-2,4-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2003:971725 CAPLUS
DOCUMENT NUMBER:	140:35893
TITLE:	Transcription factor modulating compounds and methods of use thereof
INVENTOR(S):	Levy, Stuart B.; Alekshun, Michael N.; Podlogar, Brent L.; Ohemeng, Kwasi; Verma, Atul K.; Warchol, Tadeusz; Bhatia, Beena
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 301 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	4
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030229065	A1	20031211	US 2002-139591	20020814 <--
CA 2445515	A1	20021104	CA 2002-2445515	20020506 <--
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WO 2004001058	A3	20050303		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002367953	A1	20040106	AU 2002-367953	20020506
AU 2002367953	B2	20080717		
EP 1524974	A2	20050427	EP 2002-807554	20020506

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JP 2005519998	T	20050707	JP 2004-515557		20020506
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US 7405235	B2	20080729			
AU 2008203017	A1	20080731	AU 2008-203017		20080708
PRIORITY APPLN. INFO.:			US 2001-288660P	P	20010504
			AU 2002-367953	A3	20020506
			WO 2002-US14255	W	20020506
			US 2002-139591	A2	20020814
			US 2002-423319P	P	20021101
			US 2002-425916P	P	20021113

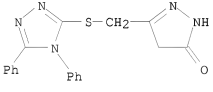
OTHER SOURCE(S): MARPAT 140:35893

AB Methods for identifying compound useful as anti-infectives that decrease resistance, virulence, or growth of microbes are provided. In one embodiment, the method comprises contacting a microbial cell comprising: (1) a selectable marker under the control of a transcription factor responsive element and (2) a transcription factor, with a compound under conditions which allow interaction of the compound with the microbial cell; and measuring the ability of the compound to affect the growth or survival of the microbial cell as an indication of whether the test compound modulates the activity of a transcription factor.

IT 305337-60-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transcription factor modulating compds. as anti-infectives agents that decrease resistance and virulence and growth identified by determining marker
under control of responsive element)

RN 305337-60-4 CAPLUS

CN 3H-Pyrazol-3-one, 5-[[(4,5-diphenyl-4H-1,2,4-triazol-3-yl)thio]methyl]-2,4-dihydro- (CA INDEX NAME)



L12 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:678811 CAPLUS

DOCUMENT NUMBER: 139:214482

TITLE: Preparation of pyrrolopyrimidine derivatives as GSK-3 inhibitors

INVENTOR(S): Kataoka, Kenichiro; Kosugi, Tomomi; Ishii, Toshihiro; Takeuchi, Takahiro; Tsutsumi, Takaharu; Nakano, Akira; Unoki, Gen; Yamamoto, Masanori; Sakai, Yuri

PATENT ASSIGNEE(S): Teijin Limited, Japan

SOURCE: PCT Int. Appl., 568 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070729	A1	20030828	WO 2003-JP1977	20030224 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

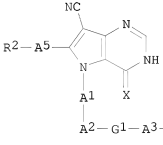
CA 2477116	A1	20030828	CA 2003-2477116	20030224 <--	
AU 2003211426	A1	20030909	AU 2003-211426	20030224 <--	
BR 2003007248	A	20041026	BR 2003-7248	20030224	
EP 1477489	A1	20041117	EP 2003-707008	20030224	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1633436	A	20050629	CN 2003-806235	20030224	
CN 100343254	C	20071017			
MX 2004006862	A	20041206	MX 2004-6862	20040715	
US 20050277773	A1	20051215	US 2004-504583	20040816	
US 7528140	B2	20090505			

PRIORITY APPLN. INFO.:

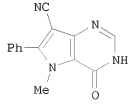
JP 2002-46128	A	20020222
JP 2002-365196	A	20021217
JP 2002-379827	A	20021227
WO 2003-JP1977	W	20030224

OTHER SOURCE(S): MARPAT 139:214482

GI



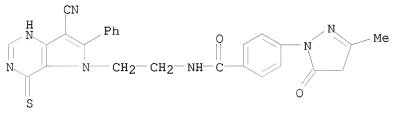
I



II

AB The title pyrrolopyrimidine derivs. with general formula of I [wherein X = O or S; A1 = a single bond or aliphatic hydrocarbyl; A2 = a single bond, CO, CO2, O, OCO, S, SO, SO2, (un)substituted CONH, CSNH, C=NH, NH, NHCO, NHSO2, NHCO2, NHCONH, NHCS, NHCSNH, or SO2NH; G1 = a single bond or (un)substituted (hetero)cyclohydrocarbyl; A3 = a single bond or aliphatic hydrocarbyl; A4 = a single bond, CO, CO2, O, OCO, S, SO, SO2, SO3, (un)substituted CONH, CSNH, C=NH, NH, NHCO, NHSO2, NHCO2, NHCONH, NHCS, NHCSNH, or SO2NH; G2 = H, or (un)substituted (hetero)(cyclo)hydrocarbyl, etc.; A5 = a single bond or (un)substituted NH; R2 = H, F, Cl, Br, I, or (un)substituted (hetero)(cyclo)hydrocarbyl, etc.] and pharmaceutically acceptable salts thereof are prepared as glycogen synthetase kinase 3 (GSK-3) inhibitors. For example, the compound II was prepared in a multi-step synthesis in good yield. Some of compds. I showed IC50 of <10 nM against GSK-3. I are useful as remedies or preventives for diseases in which GSK-3 participates such as diabetes, diabetic complications, Alzheimer's disease, neurodegenerative disease, depression, mania, traumatic brain injury, hair loss, inflammatory diseases, cancer, immunodeficiency (no data). Formulations containing I as an active ingredient were also described.

IT 587862-68-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrrolopyrimidine derivs. as GSK-3 inhibitors)
RN 587862-68-8 CAPLUS
CN Benzamide, N-[2-(7-cyano-3,4-dihydro-6-phenyl-4-thioxo-5H-pyrrolo[3,2-d]pyrimidin-5-yl)ethyl]-4-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)- (CA INDEX NAME)



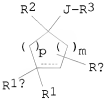
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:610206 CAPLUS
DOCUMENT NUMBER: 139:164542
TITLE: Preparation of cycloalkyl inhibitors of potassium channel function for preventing/treating arrhythmia and IKur-associated conditions
INVENTOR(S): Lloyd, John; Jeon, Yoon T.; Finlay, Heather; Yan, Lin; Gross, Michael F.; Beaudoin, Serge
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Icagen, Inc.
SOURCE: PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063797	A2	20030807	WO 2003-US3170	20030131 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2474451	A1	20030807	CA 2003-2474451	20030131 <--
US 20040072880	A1	20040415	US 2003-356158	20030131
EP 1507504	A1	20050223	EP 2003-735126	20030131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1732146	A	20060208	CN 2003-807570	20030131
JP 2006508016	T	20060309	JP 2003-563493	20030131
BR 2003007329	A	20060411	BR 2003-7329	20030131

NZ 534098	A	20070427	NZ 2003-534098		20030131
RU 2343143	C2	20090110	RU 2004-126608		20030131
IN 2004DN02052	A	20050401	IN 2004-DN2052		20040716
MX 2004007365	A	20050331	MX 2004-7365		20040729
US 20050234106	A1	20051020	US 2004-997734		20041124
US 7202253	B2	20070410			
ZA 2004005905	A	20060531	ZA 2004-5905		20060313
US 20070142333	A1	20070621	US 2007-670482		20070202
PRIORITY APPLN. INFO.:			US 2002-353884P	P	20020201
			US 2003-356158	B1	20030131
			WO 2003-US3170	W	20030131
			US 2004-997734	A3	20041124

OTHER SOURCE(S): MARPAT 139:164542
GI



AB Claimed are novel cycloalkyl compds. (shown as I; variables defined below; e.g. cis- and trans-N-(4-hydroxy-1-thiophen-2-ylcyclohexylmethyl)-2-methoxybenzamide and trans-N-[[4-[N'-cyano-N''-ethyl-N-(furan-2-ylmethyl)guanidino]-1-phenylcyclohexyl]methyl]-2-methoxybenzamide) useful as inhibitors of K channel function (especially inhibitors of the Kv1 subfamily of voltage gated K+ channels, especially inhibitors Kv1.5 which was linked to the ultra-rapidly activating delayed rectifier K+ current IKur; no data), methods of using such compds. in the prevention and treatment of arrhythmia and IKur-associated conditions, and pharmaceutical compns. containing such compds. For I: dashed line = an optional double bond, provided that R1a is absent when a double bond is present; m and p = 0-3; R1 = H, NR8C(:W)NR6R7 (W = NR8a2, NCO2R8a2, NC(O)R8a2, NCN, NSO2R8a2), NR8SO2NR6R7, etc.; R1a = H, RX; or R1 and R1a together form oxo; or R1 and R1a together with the C atom to which they are attached combine to form an (un)substituted spiro-fused heterocyclo group; or R1 and R1a together combine to form :CR8R9. R2 is heteroaryl, (heteroaryl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, alkyl, alkenyl or cycloalkyl; J is a bond, C1-4 alkylene or C1-4 alkenylene; R3 = R5 (R5 = NR6aR7a, heteroaryl, (heteroaryl)alkyl, aryl, arylalkyl, alkyl, etc.), OR5, C(:Z1)R5, OC(:Z1)R5, C(:Z1)OR5, NR8a1C(:Z1)R5, etc.; RX is one or more optional substituents, attached to any available ring carbon atom; addnl. details including provisos are given in the claims. Although the methods of preparation are not claimed, >600 example prepns. are included.

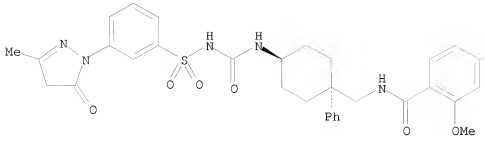
IT 577038-48-3P, cis-N-[[4-[[[[[3-(4,5-Dihydro-3-methyl-5-oxopyrazol-1-yl)phenyl]sulfonyl]amino]carbonyl]amino]-1-phenylcyclohexyl]methyl]-2-methoxybenzamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of cycloalkyl inhibitors of potassium channel function for preventing/treating arrhythmia and IKur-associated conditions)

RN 577038-48-3 CAPLUS

CN Benzamide, N-[[cis-4-[[[[[3-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)phenyl]sulfonyl]amino]carbonyl]amino]-1-phenylcyclohexyl]methyl]-2-

methoxy- (CA INDEX NAME)

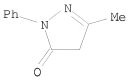
Relative stereochemistry.



L12 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:515097 CAPLUS
DOCUMENT NUMBER: 139:374549
TITLE: The free radical scavenger edaravone suppresses experimental dextran sulfate sodium-induced colitis in rats
AUTHOR(S): Araki, Yoshio; Andoh, Akira; Fujiyama, Yoshihide
CORPORATE SOURCE: Ace Bio Product Co., Chiyoda-ku, Tokyo, 101-0047, Japan
SOURCE: International Journal of Molecular Medicine (2003), 12(1), 125-129
CODEN: IJMMFG; ISSN: 1107-3756
PUBLISHER: International Journal of Molecular Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent studies suggest that the enhanced release of reactive oxygen species (ROS) plays an important role in the pathogenesis of clin. inflammatory bowel diseases (IBD) such as ulcerative colitis and Crohn's disease. In the present study, we investigated the effects of the free radical scavenger edaravone, which is used clin. as an anti-stroke agent, in the development of exptl. dextran sulfate sodium (DSS)-induced colitis in rats. The rats were fed 4% (weight/weight of diet) DSS in standard powder chow for 8 days. The edaravone and vehicle saline were injected s.c. twice a day. After the exptl. period, the wet colonic weight, macroscopic mucosal damaged area, histol. damage score, mucosal myeloperoxidase (MPO) activity, mucosal tissue lipid peroxidate and serum interleukin-6 (IL-6) levels were measured. In the DSS-induced colitis model, edaravone treatment (1-20 mg/kg day) significantly reduced the wet colonic weight, macroscopic damaged area, and the histol. damage score. Edaravone treatment also reduced mucosal MPO activity, mucosal tissue lipid peroxidate level and serum IL-6 level. In particular, edaravone at a dose of 20 mg/kg day significantly reduced mucosal MPO activity and serum IL-6 level. These results strongly support the involvement of ROS in the pathogenesis of DSS-induced colitis. A clin. effect for edaravone against IBD patients is strongly expected.

IT 89-25-8, Edaravone
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radical scavenger edaravone suppresses dextran sulfate sodium-induced colitis)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



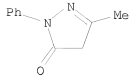
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:515096 CAPLUS
DOCUMENT NUMBER: 139:374926
TITLE: The free radical scavenger edaravone suppresses experimental closed duodenal loop-induced acute pancreatitis in rats
AUTHOR(S): Araki, Yoshio; Andoh, Akira; Yokono, Tomonobu; Asano, Nobuyuki; Yoshikawa, Kouhei; Bamba, Shigeki; Ishizuka, Izumi; Fujiyama, Yoshihide
CORPORATE SOURCE: Ace Bio Product Co., Chiyoda-ku, Tokyo, 101-0047, Japan
SOURCE: International Journal of Molecular Medicine (2003), 12(1), 121-124
CODEN: IJMMFG; ISSN: 1107-3756
PUBLISHER: International Journal of Molecular Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent studies suggest that the enhanced release of reactive oxygen species (ROS) plays an important role in the pathogenesis of clin. acute pancreatitis. In the present study, we investigated the effects of the free radical scavenger edaravone, which is used clin. as an anti-stroke agent, in the development of exptl. closed duodenal loop (CDL)-induced acute pancreatitis. In the CDL-pancreatitis model, after edaravone and vehicle saline were injected i.v., pancreatitis was induced for 7 h by the CDL technique. The subsequent ascites volume, wet pancreatic weight, serum amylase levels, and pancreatic tissue lipid peroxide levels were evaluated. Pancreatic tissue damage was also evaluated histol. In this CDL-induced pancreatitis model, edaravone treatment tended to reduce the ascites volume and inhibit the increases in the wet pancreatic weight Edaravone also tended to reduced the microscopic mucosal damage scores and pancreatic tissue lipid peroxide levels. In particular, the serum amylase levels in the edaravone-treated rats (1-20 mg/kg i.v.) were significantly reduced as compared to the vehicle-treated rats. These results strongly support the involvement of ROS in the pathogenesis of CDL-induced acute pancreatitis and cytoprotective effects of free radical scavenger against pancreatic acinar cells. A clin. effect for edaravone against acute pancreatitis is strongly expected.

IT 89-25-8, Edaravone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytoprotective effects of free radical scavenger edaravone in exptl. closed duodenal loop-induced acute pancreatitis)

RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:511337 CAPLUS
DOCUMENT NUMBER: 139:85373
TITLE: Preparation of pyrazolopyrimidinone derivatives having phosphodiesterase 7 (PDE7)-inhibitory activity
INVENTOR(S): Inoue, Hidekazu; Murafuji, Hidenobu; Hayashi, Yasuhiro
PATENT ASSIGNEE(S): Daiichi Suntory Pharma Co., Ltd., Japan; Suntory Limited; Daiichi Suntory Biomedical Research Ltd.
SOURCE: PCT Int. Appl., 244 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053975	A1	20030703	WO 2002-JP13083	20021213 <--
W: BR, CA, CN, HU, JP, KR, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
CA 2439784	A1	20030703	CA 2002-2439784	20021213 <--
BR 2002007215	A	20040210	BR 2002-7215	20021213
EP 1454897	A1	20040908	EP 2002-788833	20021213
EP 1454897	B1	20071010		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY, TR, BG, CZ, EE, SK				
CN 1533392	A	20040929	CN 2002-809154	20021213
CN 1264843	C	20060719		
HU 2004002171	A2	20050228	HU 2004-2171	20021213
HU 2004002171	A3	20080828		
AT 375347	T	20071015	AT 2002-788833	20021213
ES 2294189	T3	20080401	ES 2002-788833	20021213
US 20050148604	A1	20050707	US 2004-866198	20040614
US 7268128	B2	20070911		
PRIORITY APPLN. INFO.:			JP 2001-380483 A	20011213
			WO 2002-JP13083 W	20021213

OTHER SOURCE(S): MARPAT 139:85373
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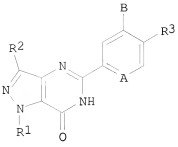

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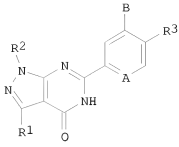
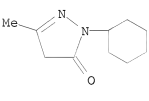


II

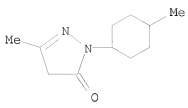
AB Pyrazolopyrimidinone derivs. represented by the general formula (I) or (II) [wherein A = N, CR4; wherein R4 = H, C1-3 alkoxy optionally substituted by ≥1 F atoms if necessary; B = H,halo; R1 = (un)substituted C3-7 cycloalkyl, tert-butyl; R2 = H, Me, Et; R3 = H, NO2, cyano, halo, NR5R6, C(:X)R7, SO2NR5R6, OR8, NR8CONR5R6, NR8SO2R9, heteroaryl, (un)substituted C1-3 alkyl; wherein R5, R6 = H, each (un)substituted C1-6 alkyl or acyl; or NR5R6 = azetidinyl, pyrrolidinyl, piperidinyl, morpholino, thiomorpholino, piperazinyl, or homopiperazinyl each optionally substituted by (un)substituted C1-4 alkyl, OH, C1-3 alkoxy, CO2H, or NR5R6; R7 = (un)substituted C1-6 alkyl, OH, OR8, NR5R6; R8 = H, (un)substituted C1-6 alkyl; R9 = (un)substituted C1-6 alkyl; X = O, S, NH] or salts or solvates thereof are prepared These compds. have .apprx.10-times more potent activity for inhibiting PDE7 than PDE4, can enhance the intracellular cAMP level by virtue of their selective inhibitory activity against PDE7, and are useful in the prevention and treatment of various allergic diseases and inflammatory and immunol. diseases through their inhibiting the activation of T cells. Thus, 207 μL N-methylpiperazine, 120 mg sodium tert-butoxide, 12.6 mg tri(tert-butylphosphine), and 7.0 mg Pd(OAc)2 were added to a solution of 260 mg 6-(4-bromo-2-methoxyphenyl)-3-cyclohexyl-1-methyl-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one in 8 mL toluene and refluxed for 5 h to give 85% 3-cyclohexyl-6-[2-methoxy-4-(4-methyl-1-piperazinyl)phenyl]-1-methyl-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one (II). II.

IT 36210-76-1P 553671-91-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazolopyrimidinone derivs. as phosphodiesterase 7 (PDE7) inhibitors for prevention and treatment of various allergic diseases and inflammatory and immunol. diseases)

RN 36210-76-1 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-methyl- (CA INDEX NAME)



RN 553671-91-3 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-(4-methylcyclohexyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:396659 CAPLUS
DOCUMENT NUMBER: 138:401613
TITLE: Preparation of tetrahydroisoquinoline analogs as modulators of chemokine receptor activity for treatment of inflammatory diseases
INVENTOR(S): Hermsmeier, Mark Alden; Rawlins, David B.; Wityak, John
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003041641	A2	20030522	WO 2002-US35779	20021107 <--
WO 2003041641	A3	20040304		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002357692	A1	20030526	AU 2002-357692		20021107 <--
US 6649606	B1	20031118	US 2002-289671		20021107 <--
PRIORITY APPLN. INFO.:			US 2001-346377P	P	20011109
			WO 2002-US35779	W	20021107

OTHER SOURCE(S): MARPAT 138:401613
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

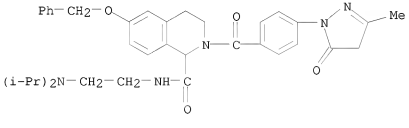
AB Title compds. I [wherein R1 = (un)substituted (aryl)alkyl, (aryl)alkenyl, alkynyl, aryl, (aryl)cycloalkyl, cycloalkylalkyl, cycloalkylalkoxy, alkoxyalkyl, alkylthioalkyl, aryloxyalkyl, arylalkoxyalkyl, heterocyclyl(alkyl), or heteroaryl(alkyl); R2 = H or (un)substituted (aryl)alkyl, (aryl)alkenyl, alkynyl, aryl, cycloalkyl(alkyl), alkoxyalkyl, cycloalkylalkoxy, aryloxyalkyl, arylalkoxyalkyl, heterocyclyl(alkyl), or heteroaryl(alkyl); X = a bond, O, or NR4; R3 and R3a = independently H,

alkoxy, halo, CF3, alkyl, or aryl; R4 = independently alkyl or aryl; m, n, and p = independently 0-1; Y = a bond, (CH2)xC6H4(CH2)y, (CH2)xCR5R5a(CH2)y, or (CH2)xCR4=CR4(CH2)z; x and y = independently 0-3; z = 1-3; R5 and R5a = independently H, (cyclo)alkyl, alkoxy, OH, halo, CF3, or (alk)aryl; or R5 and R5a may be independently joined to R6 and R7 to form an alkylene bridge; or CR5R5a = cycloalkyl; X2 = (un)substituted aryl, heterocyclyl, pyridinyl, NR6R7, or (un)substituted imidazolyl; R6 and R7 = independently H or (un)substituted alkyl; or NR6R7 = heterocyclyl; X3 = a bond, CO, CO2, CONR4, SO2, or SO2NR4; X4 = a bond, O, OCO, NR4, NR4CO, NR4CONR4, NR4SO2, NR4SO2NR4, OCONR4, CO, CONR4, S, SO2, or SO2NR4; with provisos; and enantiomers, diastereomers, and pharmaceutically acceptable salts thereof] were prepared as modulators of chemokine receptor activity (no data). For example, reaction of 3-methoxyphenethylamine with HBr gave 3-(2-aminoethyl)phenol•HBr (100%). Cyclization with glyoxylic acid monohydrate in a 5% HCl solution, followed by esterification with MeOH provided Me 6-hydroxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (35%). N-protection with di-tert-Bu dicarbonate in THF, etherification with benzyl bromide using K2CO3 in DMF (93%), and saponification using NaOH in H2O and MeOH afforded 6-(benzyloxy)-1,2,3,4-tetrahydroisoquinoline-1,2-dicarboxylic acid 2-tert-Bu ester (83%). Amidation with diisopropylethylenediamine in the presence of 1-hydroxy-7-azabenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide•HCl in DMF gave II (79%). Thus, I and compns. containing I are useful for the treatment of inflammatory diseases, such as asthma, COPD, allergic disease, allergic rhinitis, rheumatoid arthritis, atherosclerosis, psoriasis, solid organ transplant rejection, osteoarthritis, and inflammatory bowel syndrome (no data).

IT 373636-28-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiinflammatory; preparation of tetrahydroisoquinoline analogs as modulators of chemokine receptor activity for treatment of inflammatory diseases)

RN 373636-28-3 CAPLUS

CN 1-Isoquinolinecarboxamide, N-[2-[bis(1-methylethyl)amino]ethyl]-2-[4-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)benzoyl]-1,2,3,4-tetrahydro-6-(phenylmethoxy)- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

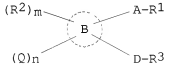
L12 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:154382 CAPLUS
DOCUMENT NUMBER: 138:187795
TITLE: Preparation of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivatives as antagonists of prostaglandin E2 (PEG2) receptors
INVENTOR(S): Tani, Kousuke; Asada, Masaki; Kobayashi, Kaoru;

Narita, Masami; Ogawa, Mikio
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 1009 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016254	A1	20030227	WO 2002-JP8120	20020808 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2457468	A1	20030227	CA 2002-2457468	20020808 <--
AU 2002323916	A1	20030303	AU 2002-323916	20020808 <--
EP 1431267	A1	20040623	EP 2002-755874	20020808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011810	A	20040824	BR 2002-11810	20020808
CN 1551866	A	20041201	CN 2002-817376	20020808
HU 2004001963	A2	20050128	HU 2004-1963	20020808
HU 2004001963	A3	20060130		
NZ 531153	A	20051028	NZ 2002-531153	20020808
NZ 541950	A	20070223	NZ 2002-541950	20020808
RU 2315746	C2	20080127	RU 2004-106623	20020808
CN 101284773	A	20081015	CN 2008-10002260	20020808
ZA 2004000973	A	20050104	ZA 2004-973	20040205
NO 2004000564	A	20040510	NO 2004-564	20040206
MX 2004001253	A	20040603	MX 2004-1253	20040209
US 20060258728	A1	20061116	US 2004-486220	20040909
US 7491748	B2	20090217		

PRIORITY APPLN. INFO.:			
	JP 2001-241867	A	20010809
	CN 2002-817376	A3	20020808
	WO 2002-JP8120	W	20020808

OTHER SOURCE(S): MARPAT 138:187795
GI



I

AB Carboxylic acid derivs. (I) and nontoxic salts thereof [wherein R1 = CO2H, CO2R4, CH2OH, COR5SO2R6, CONH2, CH2NR5SO2R6, CH2NR9COR10, CH2NR9CONR5SO2R6, CH2SO2NR9COR10, CH2O2CNR5SO2R6, tetrazole, 1,2,4-oxadiazol-5-one, 1,2,4-oxadiazol-5-thione, 1,2,4-thiadiazol-5-one, etc. (wherein R4 = C1-6 alkyl, hydroxy-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, carboxy-C1-4 alkyl, etc.; R5, R9 = H, C1-6 alkyl; R6 = C1-6 alkyl, C3-15 mono-, di-, or tricarbocyclic, 3- to 13-membered mono-, di-, or tricyclic

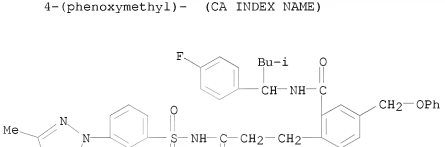
heterocyclyl, etc.; R10 = H, R6); A = a single bond, C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, etc.; the ring B = C3-12 mono- or dicyclic carbocyclic ring, 3- to 12-membered mono- or dicyclic heterocyclic ring; R2 = C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C2-6 alkenyl, C2-6 alkynyl, halo, CHF2, CF3, NO2, cyano, Ph, oxo; m, n = 0,1,2; Q = (C1-4 alkylene, C2-4 alkenylene, or C2-4 alkynylene)-Cyc2, -C1-4 alkylene-Z-Cyc3, amino-C1-4 alkyl, cyano-C1-4 alkyl, acylamino-C1-4 alkyl, 3- to 7-membered monocyclic carbocyclyl, 3- to 6-membered monocyclic heterocyclyl, etc. (wherein Cyc2, Cyc3 = C3-15 mono-, di-, or tricyclic carbocyclyl or heterocyclyl, etc.; Z = O, S, SO, SO2, NH, NHCO, etc.); D = an linking chain consisting of 1-2 or 3-6 of atoms selected from C, N, O, or S, etc.; R3 = C1-6 alkyl, C3-15 mono-, di-, or tricyclic carbocyclyl, 3- to 15-membered mono-, di-, or tricyclic heterocyclyl, etc.] are prepared These carboxylic acid derivs. include phenylpropanoic acid, phenylpropenoic acid, phenylpropanamide, phenylpropenamide, 3-oxoisoindolin-1-ylacetic acid, benzylbenzoic acid, benzylaminoacetic acid, pyrazolylmethylbenzoic acid, benzoylaminoacetic acid, (pyrazolylmethylphenyl)propenoic acid, pyrazolylmethylpropanoic acid, (pyridinyloxyphenyl)propanoic acid, phenoxyacetic acid, phenylbutanoic acid, (pyrazolylmethyl)propanamide, (piperazinylmethylphenyl)propanamide, (morpholinylmethylphenyl)propanamide, (pyridinyloxyphenyl)propanamide, (pyrazolylmethyl)propenamide (oxoimidazolidinylmethylphenyl)propanamide, (oxopyrrolidinylmethylphenyl)propenamide, (thiophenylmethylphenyl)propenamide, (pyrazolylmethylphenylamino)acetamide, (thiazolylaminomethylphenyl)propanamide, thiophenylpropenamide, (pyrazolylmethylphenoxy)acetamide, (phenoxymethyl)benzamide, (pyrazolylmethylphenylethyl)-1,2,4-oxadiazol-5-one, and (pyrazolylmethylphenylindolyl)acetic acid. Because of binding to PEG2 receptors, in particular, subtype EP3 and/or subtype EP4 and having antagonism, the compds. I are useful in preventing and/or treating diseases such as pain, allodynia, hyperalgesia, pruritus (itching), urticaria, atopic dermatitis, contact dermatitis, Urushi (Japanese lacquer tree) dermatitis, allergic conjunctivitis, symptoms during dialysis, asthma, rhinitis, allergic rhinitis, nasal congestion, sneeze, psoriasis, pollakiuria (increased urinary frequency), urination disorder, ejaculation (semination) disorder, fever (pyrexia), systemic inflammation reaction, learning disorder, Alzheimer's disease, neovascularization, cancer formation, cancer proliferation, cancer metastasis to organs, cancer metastasis to bone, hypercalcemia accompanied by cancer metastasis to bone, retinopathy, rubrum, erythema (rash), leucoma, skin moth-patch, heat burn, burn, steroid burn, kidney failure, nephropathy, acute or chronic nephritis, blood electrolyte disorder, imminent abortion, threatened abortion, excessive menstruation, dysmenorrhea, endometriosis, premenstrual syndrome, uterine gland myopathy, reproduction disorder, and stress. They are also useful in preventing and/or treating anxiety, depression, psychophysiol. disorder, mental retardation, thrombus, embolism, transient ischemic attack, cerebral infarction, atheroma, organ transplant, heart failure, hypertension, myocardial infarction, arteriosclerosis, circulation disorders or ulcers associated therewith, nerve disorders, vascular dementia, edema, diarrhea, constipation, biliary excretion disorder, ulcerative colitis, Crohn's disease, irritable bowel syndrome, reduction of rebound after using steroid drugs, aids for decreasing or removing steroid drugs, bone diseases, systemic granuloma, immune diseases, pyorrhea alveolaris, gingivitis, periodontal disease, nerve cell death, lung disorder, liver disorder, acute hepatitis, myocardial ischemia, Kawasaki disease, multiple organ failure, chronic headache, angiitis, venous failure, varicose vein (varicosis), anal fistula, diabetes insipidus, neonatal patent ductus arteriosus, and cholelithiasis. Thus, 4-hydroxymethyl-2-[2-(naphthalen-2-yl)ethoxy]cinnamic acid Et ester was mesylated by methanesulfonyl chloride in the presence of Et3N in THF at 0° for 15 min and condensed with pyrazole in the presence of NaH

in DMF at 0° to give 2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid Et ester. 4-[2-[[2-(Naphthalen-1-yl)propanoyl]amino]-4-methylthiomethylphenyl]butanoic acid inhibited the binding of [3H]PGE2 to prostaglandin E2 (PEG2) receptor subtype EP1, Ep2, EP3, and EP4 expressed in CHO cells with Ki of >10, >10, 0.27, and 0.038 μM, resp. A tablet formulation containing (2E)-2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid was described.

IT 499152-34-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivs. as antagonists of prostaglandin E2 (PEG2) receptors as therapeutic agents)

RN 499152-34-0 CAPLUS

CN Benzenepropanamide, N-[[3-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)phenyl]sulfonyl]-2-[[[1-(4-fluorophenyl)-3-methylbutyl]amino]carbonyl]-4-(phenoxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:117622 CAPLUS
DOCUMENT NUMBER: 138:170229
TITLE: Preparation of pyrazolone derivatives as inhibitors of GSK-3, Aurora-2 and CDK-2
INVENTOR(S): Green, Jeremy; Arnost, Michael J.; Pierce, Albert
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011287	A1	20030213	WO 2002-US24726	20020802 <--

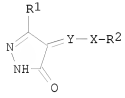
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,

NE, SN, TD, TG

AU 2002330983	A1	20030217	AU 2002-330983	20020802	<--
US 20040024040	A1	20040205	US 2002-212471	20020802	
US 6916798	B2	20050712			
US 20050222237	A1	20051006	US 2005-145356	20050603	
US 7452873	B2	20081118			
PRIORITY APPLN. INFO.:			US 2001-309838P	P 20010803	
			US 2002-212471	A3 20020802	
			WO 2002-US24726	W 20020802	

OTHER SOURCE(S): MARPAT 138:170229
GI



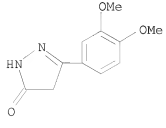
I

AB The present invention relates to pyrazolones (shown as I; variables defined below; e.g. 4-[(3-benzyloxyphenylamino)methylene]-5-(3,4-dimethoxyphenyl)-2,4-dihydropyrazol-3-one) that are useful as glycogen synthase kinase-3, Aurora-2 protein kinase and cyclin-dependent kinase-2 inhibitors (pharmacol. results included). The invention also relates to methods of using I or pharmaceutical compns. comprising I to inhibit the enzymes. The invention further provides methods of using these compds. and pharmaceutical compns. in the treatment and prevention of various disorders, such as diabetes and Alzheimer's disease. Although the methods of preparation are not claimed, .apprx.12 example prepns. are included and characterization data are included for .apprx.200 I. For I: R1 = H, alkyl, carbocyclyl, heterocyclyl, aryl, heteroaryl, -CN, -C(O)R, -CO2R, or -CON(R)2; R2 = H, alkyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl; X is O, S or -NH; Y is N or CH; each R = H, alkyl, carbocyclyl, heterocyclyl, aryl, heteroaryl, or any two R groups taken together form a carbocyclyl, heterocyclyl, aryl or heteroaryl group; each R' = H, alkyl, carbocyclyl, heterocyclyl, aryl, heteroaryl, or any two R' groups taken together form a carbocyclyl, heterocyclyl, aryl or heteroaryl group; addnl. conditions are given in the claims.

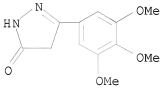
IT 264208-47-1, 5-(3,4-Dimethoxyphenyl)-2,4-dihydro-3H-pyrazol-3-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrazolone derivs. as inhibitors of GSK-3, Aurora-2 and CDK-2)

RN 264208-47-1 CAPLUS

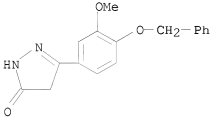
CN 3H-Pyrazol-3-one, 5-(3,4-dimethoxyphenyl)-2,4-dihydro- (CA INDEX NAME)



IT 1575-01-5P, 5-(3,4,5-Trimethoxyphenyl)-2,4-dihydro-3H-pyrazol-3-one 496934-45-3P, 5-(4-Benzyloxy-3-methoxyphenyl)-2,4-dihydro-3H-pyrazol-3-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazolone derivs. as inhibitors of GSK-3, Aurora-2 and CDK-2)
RN 1575-01-5 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-(3,4,5-trimethoxyphenyl)- (CA INDEX NAME)



RN 496934-45-3 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-[3-methoxy-4-(phenylmethoxy)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:97274 CAPLUS
DOCUMENT NUMBER: 138:153318
TITLE: Preparation of substituted phenols as cytoprotective agents useful in pharmaceutical and cosmetic formulations
INVENTOR(S): Wang, Bing; Zhang, Yong-Kang; Chen, Jian; Zhang, Wei; Song, Jiangao; Del, Balzo Ughetta; Brown, Lesley; Miller, Guy
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003009807	A2	20030206	WO 2002-US23509	20020723 <--
WO 2003009807	A3	20040429		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2452159	A1	20030206	CA 2002-2452159	20020723	<--
AU 2002319677	A1	20030217	AU 2002-319677	20020723	<--
AU 2002319677	B2	20090326			
US 20030073712	A1	20030417	US 2002-202670	20020723	<--
EP 1435894	A2	20040714	EP 2002-750281	20020723	
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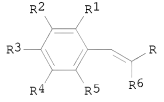
JP 2005505519	T	20050224	JP 2003-515200	20020723	
MX 2004000695	A	20050826	MX 2004-695	20040122	
US 20050113416	A1	20050526	US 2004-15198	20041216	
US 20050142155	A1	20050630	US 2005-55895	20050210	
US 20060178356	A1	20060810	US 2006-387507	20060322	

PRIORITY APPLN. INFO.:	US 2001-307439P	P	20010723
	US 2002-353702P	P	20020131
	US 2002-202670	A3	20020723
	WO 2002-US23509	W	20020723

OTHER SOURCE(S): MARPAT 138:153318
GI



I

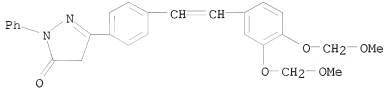
AB Phenolic derivs. having conjugated bonds I [wherein R = NO2, substituted alkenyl, or (un)substituted aryl(carbonyl), heteroaryl, or heterocyclyl; R1-R5 = independently H, carboxy, CN, halo, OH, NO2, nitrone, sulfonate, or (un)substituted alkoxy(carbonyl), alkenyl, alkyl, or (hetero)aryl; or 2 adjacent members of R1 to R5 = O- and together complex with C or a metal; provided that at least 1 of R1 to R5 = MeOCH2O or H(CH2CMe=CHCH2)n; n = 1-4; further provided that when R1 to R5 = MeOCH2O, R = Ph para-substituted by CN, NO2, nitroso, NHOH, NH2CO, alkyl ester, N-containing heterocyclyl, etc.; R6 = H or (un)substituted alkoxycarbonyl; or stereoisomers or pharmaceutically acceptable salts thereof] were prepared as cytoprotective agents useful in pharmaceutical and cosmetic formulations. For example, coupling of (4-nitrobenzyl)triphenylphosphonium bromide with 3,4-bis(methoxymethoxy)benzaldehyde using LiOEt in EtOH (41%) followed by deetherification with concentrated HCl in EtOH gave 4-[2-(4-nitrophenyl)vinyl]benzene-1,2-diol (81%). The latter was among invention compds. that showed significant reduction in edema in assays assessing rat paw edema (10 to 70%, $p < 0.05$) and mouse ear inflammatory response to topical arachidonic acid (15 to 80%, $p < 0.05$). Results from the neuronal cell stress assay and the rat middle cerebral artery occlusion model of cerebral ischemia were also disclosed for selected invention compds. Thus, I are useful in the treatment of certain ischemic or inflammatory conditions, including but not limited to stroke, myocardial infarction, congestive heart failure, and skin disorders characterized by inflammation or oxidative damage.

IT 495412-64-1P, 5-[4-[2-[3,4-Bis(methoxymethoxy)phenyl]vinyl]phenyl]-2-phenyl-2,4-dihydropyrazol-3-one

RL: COS (Cosmetic use); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(cytoprotectant; preparation of substituted phenols as cytoprotective agents useful in pharmaceutical and cosmetic formulations for treating ischemic or inflammatory conditions)

RN 495412-64-1 CAPLUS

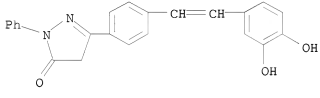
CN 3H-Pyrazol-3-one, 5-[4-[2-[3,4-bis(methoxymethoxy)phenyl]ethenyl]phenyl]-2,4-dihydro-2-phenyl- (CA INDEX NAME)



IT 495412-66-3P, 5-[4-[2-(3,4-Dihydroxyphenyl)vinyl]phenyl]-2-phenyl-2,4-dihydropyrazol-3-one 495412-67-4P, 2-[4-[2-(4-Hydroxy-3-methoxyphenyl)vinyl]phenyl]-5-methyl-2,4-dihydropyrazol-3-one 495412-70-9P, 5-Methyl-2-(4-styrylphenyl)-2,4-dihydropyrazol-3-one
RL: COS (Cosmetic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cytoprotectant; preparation of substituted phenols as cytoprotective agents useful in pharmaceutical and cosmetic formulations for treating ischemic or inflammatory conditions)

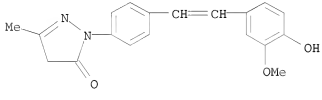
RN 495412-66-3 CAPLUS

CN 3H-Pyrazol-3-one, 5-[4-[2-(3,4-dihydroxyphenyl)ethenyl]phenyl]-2,4-dihydro-2-phenyl- (CA INDEX NAME)



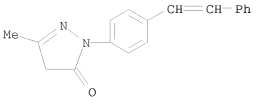
RN 495412-67-4 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-2-[4-[2-(4-hydroxy-3-methoxyphenyl)ethenyl]phenyl]-5-methyl- (CA INDEX NAME)

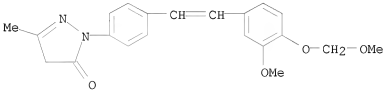


RN 495412-70-9 CAPLUS

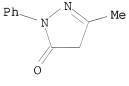
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-[4-(2-phenylethenyl)phenyl]- (CA INDEX NAME)



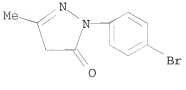
IT 495412-69-6P, 2-[4-[2-(3-Methoxy-4-methoxymethoxyphenyl)vinyl]phenyl]-5-methyl-2,4-dihydropyrazol-3-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of substituted phenols as cytoprotective agents useful in pharmaceutical and cosmetic formulations for treating ischemic or inflammatory conditions)
RN 495412-69-6 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-[4-[2-[3-methoxy-4-(methoxymethoxy)phenyl]ethenyl]phenyl]-5-methyl- (CA INDEX NAME)



IT 89-25-8, 3-Methyl-1-phenyl-2-pyrazolin-5-one 14580-15-5, 2-(4-Bromophenyl)-5-methyl-2,4-dihydropyrazol-3-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted phenols as cytoprotective agents useful in pharmaceutical and cosmetic formulations for treating ischemic or inflammatory conditions)
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



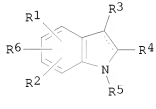
RN 14580-15-5 CAPLUS
CN 3H-Pyrazol-3-one, 2-(4-bromophenyl)-2,4-dihydro-5-methyl- (CA INDEX NAME)



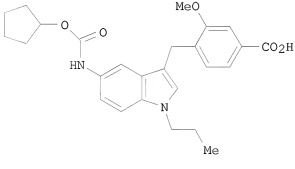
ACCESSION NUMBER: 2003:1275 CAPLUS
DOCUMENT NUMBER: 138:55866
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors for treatment of inflammatory conditions
INVENTOR(S): Seehra, Jasbir S.; McKew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.
PATENT ASSIGNEE(S): Genetics Institute, LLC, USA
SOURCE: U.S., 57 pp., Cont.-in-part of U. S. Ser. No. 256,062, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6500853	B1	20021231	US 2000-686616		20001011 <--
PRIORITY APPLN. INFO.:			US 1998-113674P	P	19980228
			US 1999-256062	B2	19990224

OTHER SOURCE(S): MARPAT 138:55866
GI



I



II

AB Title compds. I [wherein R1 and R6 = independently H, halo, CF3, alkyl, alkylthio, alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halo, CF3, OH, alkyl, alkoxy, CHO, CN, NO2, (un)substituted amino, or alkylsulfonyl; R3 = CO2H, OPO3H2, SO3H, etc.; R4 = H, CF3, alkyl, alkoxy, (alkyl)cycloalkyl, CHO, halo, etc.; R5 = alkyl, alkoxy, (alkyl)cycloalkyl, etc.; and pharmaceutically acceptable salts thereof] were prepared as phospholipase enzyme inhibitors. For example, 5-nitroindole was C3-alkylated (55%) with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated (57%) with 1-iodopropane in a solution of THF and NaH, and converted to the amine (80%) by hydrogenation using Pt/C. The amine was converted to the carbamate (39%) by addition of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine, and the resultant ester was hydrolyzed to yield II

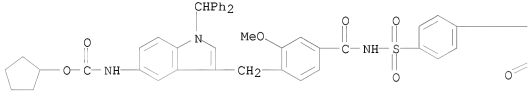
(71%). The latter inhibited cytosolic phospholipase A2 (cPLA2) by 50% at a concentration of 170 μM in a coumarin assay and reduced footpad volume by 16.61% at a dose of 5 mg/Kg IV in a carrageenan-induced footpad edema test on rats. Thus, I are useful for treatment of inflammatory conditions, such as arthritis, inflammatory bowel disease, and asthma (no data).

IT 241497-10-9P, Carbamic acid, [3-[[4-[[[[4-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)phenyl]sulfonyl]amino]carbonyl]-2-methoxyphenyl]methyl]-1-(diphenylmethyl)-1H-indol-5-yl]-, cyclopentyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phospholipase inhibitor; preparation of indole derivs. as phospholipase enzyme inhibitors for treatment of inflammatory conditions)

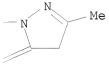
RN 241497-10-9 CAPLUS

CN Carbamic acid, [3-[[4-[[[[4-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)phenyl]sulfonyl]amino]carbonyl]-2-methoxyphenyl]methyl]-1-(diphenylmethyl)-1H-indol-5-yl]-, cyclopentyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

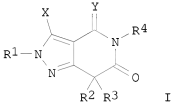
L12 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2002:849627 CAPLUS
DOCUMENT NUMBER:	137:370084
TITLE:	Preparation of 4,5,6,7-tetrahydropyrazolo[4,3-c]pyridine-4,6-dione derivatives as inhibitors of production of tumor necrosis factor-α (TNF-α)
INVENTOR(S):	Tanaka, Yasuhiro; Fujita, Kohichi; Chujoh, Yoshitomo; Fukuda, Syunsuke; Ikenoue, Yuka; Tagami, Tomoyuki; Chiba, Akira; Kodaira, Ariko; Matsumoto, Hideki; Nakagawa, Tadakiyo; Yamada, Tatsuhiro; Suzuki, Manabu; Murata, Masahiro
PATENT ASSIGNEE(S):	Ajinomoto Co., Inc., Japan
SOURCE:	PCT Int. Appl., 116 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088122	A1	20021107	WO 2002-JP4206	20020426 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002251553	A1	20021111	AU 2002-251553	20020426 <--
EP 1396493	A1	20040310	EP 2002-720620	20020426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 4196678	B2	20081217	JP 2002-585421	20020426
US 20040147546	A1	20040729	US 2004-475097	20040224
PRIORITY APPLN. INFO.:			JP 2001-130438 A	20010426
			WO 2002-JP4206 W	20020426

OTHER SOURCE(S): MARPAT 137:370084

GI



I

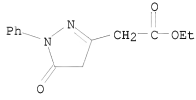
AB Pharmaceutical compns. containing as the active ingredient heterocyclic compds. represented by the general formula (I), isomers or solvates thereof, or pharmaceutically acceptable salts of them [R1 = each (un)substituted alkyl, cycloalkyl, cycloalkylalkyl, aralkyl, aryl, heteroaryl, heteroarylalkyl, or cycloalkyl or cycloalkylalkyl each optionally containing a heteroatom in the ring; R2, R3 = H, HO, or each (un)substituted alkyl or aralkyl; or R2 and R3 together represent cycloalkyl optionally containing a heteroatom in the ring, :CR5R6, :N+(O-)R7, :NR8, or oxo [wherein R5, R6 = H, alkoxyl, alkoxycarbonyl, each (un)substituted alkyl, cycloalkyl, aralkyl, aryl, heteroaryl, or cycloalkyl; R7 = (un)substituted aryl; R8 = HO, alkoxy, each (un)substituted aryl or heteroaryl; R9 = (un)substituted aryl or heteroaryl, acyl, CONH2]; R4 = H, each (un)substituted alkyl or aralkyl; X = H, halo, HO, each (un)substituted alkyl, aralkyl, alkoxy, aryl, heteroaryl, NH2, alkylthio, aralkylthio, arylthio, heteroarylthio, alkylsulfonyl, aralkylsulfonyl, arylsulfonyl, etc.; Y = O, S] are disclosed. These compds. exhibit excellent TNF-α production inhibiting activity and are therefore useful in the prevention and treatment of various diseases caused by abnormal production of TNF-α such as Crohn's disease, ulcerative colitis, septicemia, chronic articular rheumatism, or autoimmune disease. Thus, 3-amino-2-phenyl-2H-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridine-4,6-dione and pentafluorobenzaldehyde were refluxed in the presence of a catalytic amount of AcOH in ethanol overnight to give 3-amino-7-(2,3,4,5,6-pentafluorobenzylidene)-2-phenyl-2H-4,5,6,7-

tetrahydropyrazolo[4,3-c]pyridine-4,6-dione (II). II showed IC50 of 0.4 μM for inhibiting the lipopolysaccharide-stimulated production of TNF-α in mouse i.p. macrophage.

IT 29211-44-7, Ethyl (5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)acetate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tetrahydropyrazolo[4,3-c]pyridinedione derivs. as TNF-α production inhibitors for prevention and treatment of various diseases caused by abnormal production of TNF-α)

RN 29211-44-7 CAPLUS

CN 1H-Pyrazole-3-acetic acid, 4,5-dihydro-5-oxo-1-phenyl-, ethyl ester (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2002:814851 CAPLUS
DOCUMENT NUMBER:	137:310930
TITLE:	Preparation of 3-(azahetero)aryl-1H-pyrazolo[3,4-d]pyrimidin-3-amines as protein kinase inhibitors with antiangiogenic properties
INVENTOR(S):	Hirst, Gavin C.; Rafferty, Paul; Ritter, Kurt; Calderwood, David; Wishart, Neil; Arnold, Lee D.; Friedman, Michael M.
PATENT ASSIGNEE(S):	Abbott Laboratories, USA
SOURCE:	U.S. Pat. Appl. Publ., 426 pp., Cont.-in-part of U.S. Ser. No. 663,780. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

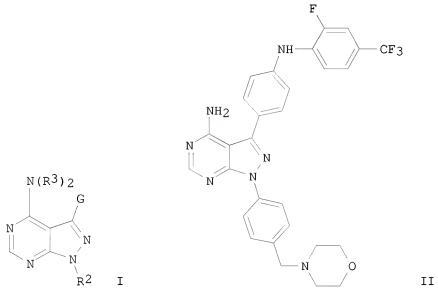
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020156081	A1	20021024	US 2001-815310	20010322 <--
US 6921763	B2	20050726		
US 6660744	B1	20031209	US 2000-663780	20000915 <--
CA 2440724	A1	20021017	CA 2002-2440724	20020322 <--
WO 2002080926	A1	20021017	WO 2002-US9104	20020322 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002316030	A1	20021021	AU 2002-316030	20020322 <--

EP 1385524	A1	20040204	EP 2002-746301		20020322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
CN 1520298	A	20040811	CN 2002-810250		20020322
JP 2004531513	T	20041014	JP 2002-578965		20020322
BR 2002005889	A	20041109	BR 2002-5889		20020322
ZA 2003006886	A	20040716	ZA 2003-6886		20030903
MX 2003008561	A	20040630	MX 2003-8561		20030922
IN 2003MN00935	A	20050429	IN 2003-MN935		20031003
BG 108269	A	20041230	BG 2003-108269		20031014
PRIORITY APPLN. INFO.:			US 1999-154620P	P	19990917
			US 2000-663780	A2	20000915
			US 2001-815310	A	20010322
			WO 2002-US9104	W	20020322

OTHER SOURCE(S): MARPAT 137:310930

GI



AB Title compds. I [wherein G = (un)substituted 5-6 membered (azahetero)aryl; R2 = H or (un)substituted trityl, cycloalkenyl, azaheteroaryl, or C6H4-4-CH2E; E = (un)substituted alkyl-OR, alkyl-CO2R, alkylheteroaryl, alkylheterocycloalkyl, or alkyl-NR2; R = independently H or (un)substituted (cyclo)alkyl, or aryl(alkyl); R3 = independently H, OH, or (un)substituted alkyl, alkyl-CO, (hetero)aryl-CO, or alkoxy; or racemic diastereomeric mixts., optical isomers, pharmaceutically acceptable salts, prodrugs, and/or biol. active metabolites thereof] were prepared For example, 3-iodo-1H-pyrazolo[3,4-d]pyrimidin-4-amine was coupled with 4-fluorobenzaldehyde in the presence of NaH in DMF to give 4-(4-amino-3-iodo-1H-pyrazolo[3,4-d]pyrimidin-1-yl)benzaldehyde. Treatment of the 3-iodopyrazolopyrimidine with N-[2-methoxy-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-2-fluoro-4-(trifluoromethyl)benzamide, Pd(PPh3)4, and Na2CO3 in H2O afforded the N-[4-(pyrazolopyrimidin-3-yl)phenyl]benzamide. Addition of morpholine to the benzaldehyde in the presence of Na(AcO)3BH in dichloroethane produced II. All exemplified compds. significantly inhibited either FGFR, PDGFR, KDR, Tie-2, Lck, Fyn, Blk, Lyn, or Src at concentration of ≤ 50 μM. Certain compds. of the invention also significantly inhibited cdc2 or cellular VEGF-induced KDR tyrosine kinase phosphorylation at concns. of ≤ 50 μM. Thus, I are useful for the treatment of a

wide variety of disease states ameliorated by the inhibition of protein tyrosine kinase activity essential for angiogenic processes (no data). [This abstract record is one of 2 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

IT 330792-35-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; preparation of [(hetero)aryl]pyrazolo[3,4-d]pyrimidinamines as protein kinase inhibitors with antiangiogenic properties)

RN 330792-35-3 CAPLUS

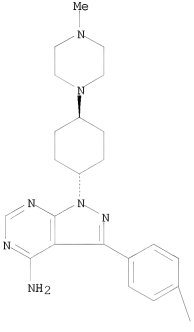
CN 3H-Pyrazol-3-one, 2-[4-[4-amino-1-[trans-4-(4-methyl-1-piperazinyl)cyclohexyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl]phenyl]-2,4-dihydro-5-methyl-, acetate (1:2) (CA INDEX NAME)

CM 1

CRN 330792-34-2
CMF C26 H33 N9 O

Relative stereochemistry.

PAGE 1-A



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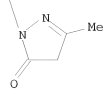


CM 2

CRN 64-19-7
CMF C2 H4 O2

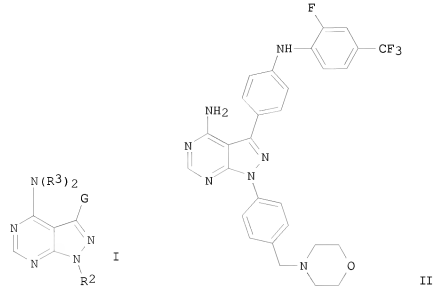
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:793426 CAPLUS
DOCUMENT NUMBER: 137:310925
TITLE: Preparation of 3-(azahetero)aryl-1H-pyrazolo[3,4-d]pyrimidin-3-amines as protein kinase inhibitors with antiangiogenic properties
INVENTOR(S): Hirst, Gavin C.; Rafferty, Paul; Ritter, Kurt; Calderwood, David; Wishart, Neil; Arnold, Lee D.; Friedman, Michael M.
PATENT ASSIGNEE(S): Abbott G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 867 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080926	A1	20021017	WO 2002-US9104	20020322 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20020156081	A1	20021024	US 2001-815310	20010322 <--
US 6921763	B2	20050726		
CA 2440724	A1	20021017	CA 2002-2440724	20020322 <--
AU 2002316030	A1	20021021	AU 2002-316030	20020322 <--
EP 1385524	A1	20040204	EP 2002-746301	20020322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004531513	T	20041014	JP 2002-578965	20020322
BR 2002005889	A	20041109	BR 2002-5889	20020322
MX 2003008561	A	20040630	MX 2003-8561	20030922
IN 2003MN00935	A	20050429	IN 2003-MN935	20031003
PRIORITY APPLN. INFO.:			US 2001-815310	A 20010322
			US 1999-154620P	P 19990917
			US 2000-663780	A2 20000915
			WO 2002-US9104	W 20020322

OTHER SOURCE(S): MARPAT 137:310925

GI



AB Title compds. I [wherein G = (un)substituted 5-6 membered (azahetero)aryl; R2 = H or (un)substituted trityl, cycloalkenyl, azaheteroaryl, or C6H4-4-CH2E; E = (un)substituted alkyl-OR, alkyl-CO2R, alkylheteroaryl, alkylheterocycloalkyl, or alkyl-NR2; R = independently H or (un)substituted (cyclo)alkyl, or aryl(alkyl); R3 = independently H, OH, or (un)substituted alkyl, alkyl-CO, (hetero)aryl-CO, or alkoxy; or racemic diastereomeric mixts., optical isomers, pharmaceutically acceptable salts, prodrugs, and/or biol. active metabolites thereof] were prepared For example, 3-iodo-1H-pyrazolo[3,4-d]pyrimidin-4-amine was coupled with 4-fluorobenzaldehyde in the presence of NaH in DMF to give 4-(4-amino-3-iodo-1H-pyrazolo[3,4-d]pyrimidin-1-yl)benzaldehyde. Treatment of the 3-iodopyrazolopyrimidine with N-[2-methoxy-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-2-fluoro-4-(trifluoromethyl)benzamide, Pd(PPh3)4, and Na2CO3 in H2O afforded the N-[4-(pyrazolopyrimidin-3-yl)phenyl]benzamide. Addition of morpholine to the benzaldehyde in the presence of Na(AcO)3BH in dichloroethane produced II. All exemplified compds. significantly inhibited either FGFR, PDGFR, KDR, Tie-2, Lck, Fyn, Blk, Lyn, or Src at concentration of ≤ 50 μM. Certain compds. of the invention also significantly inhibited cdc2 or cellular VEGF-induced KDR tyrosine kinase phosphorylation at concns. of ≤ 50 μM. Thus, I are useful for the treatment of a wide variety of disease states ameliorated by the inhibition of protein tyrosine kinase activity essential for angiogenic processes (no data).

IT 330792-35-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; preparation of [(hetero)aryl]pyrazolo[3,4-d]pyrimidinamines as protein kinase inhibitors with antiangiogenic properties)

RN 330792-35-3 CAPLUS

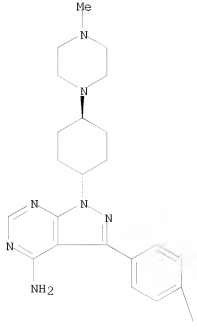
CN 3H-Pyrazol-3-one, 2-[4-[4-amino-1-[trans-4-(4-methyl-1-piperazinyl)cyclohexyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl]phenyl]-2,4-dihydro-5-methyl-, acetate (1:2) (CA INDEX NAME)

CM 1

CRN 330792-34-2
CMF C26 H33 N9 O

Relative stereochemistry.

PAGE 1-A



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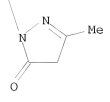

CM 2

CRN 64-19-7
CMF C2 H4 O2

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 30 CAPLUS

ACCESSION NUMBER: 2002:637680 CAPLUS
DOCUMENT NUMBER: 137:185502
TITLE: Preparation of 2,6-disubstituted 7-oxopyrido[2,3-d]pyrimidines for treating p38 mediated disorders
INVENTOR(S): Chen, Jian Jeffrey; Dunn, James Patrick; Goldstein, David Michael; Stahl, Christoph Martin
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2002064594	A2	20020822	WO 2002-EP1106	20020204	<--
WO 2002064594	A3	20030109			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2434834	A1	20020822	CA 2002-2434834	20020204	<--
AU 2002256615	A1	20020828	AU 2002-256615	20020204	<--
AU 2002256615	B2	20070913			
EP 1361880	A2	20031119	EP 2002-726103	20020204	<--
EP 1361880	B1	20050928			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 2003003458	A2	20040128	HU 2003-3458	20020204	
BR 2002007172	A	20040330	BR 2002-7172	20020204	
CN 1503672	A	20040609	CN 2002-804834	20020204	
CN 100376571	C	20080326			
JP 2004525896	T	20040826	JP 2002-564525	20020204	
JP 4064818	B2	20080319			
NZ 526961	A	20050324	NZ 2002-526961	20020204	
AT 305303	T	20051015	AT 2002-726103	20020204	
RU 2269527	C2	20060210	RU 2003-125887	20020204	
ES 2249574	T3	20060401	ES 2002-726103	20020204	
US 20030171584	A1	20030911	US 2002-73845	20020211	<--
US 6696566	B2	20040224			
ZA 2003005938	A	20041101	ZA 2003-5938	20030731	
HR 2003000624	B1	20070331	HR 2003-624	20030801	
IN 2003CN01234	A	20051118	IN 2003-CN1234	20030808	
MX 2003007166	A	20031118	MX 2003-7166	20030811	<--
NO 326133	B1	20081006	NO 2003-3540	20030811	
BG 108085	A	20041230	BG 2003-108085	20030812	
US 20040116698	A1	20040617	US 2003-722703	20031125	
US 7169794	B2	20070130			
HK 1066170	A1	20080523	HK 2004-109141	20041119	
US 20070135458	A1	20070614	US 2007-651302	20070109	
US 7449581	B2	20081111			

PRIORITY APPLN. INFO.:			
	US 2001-268375P	P	20010212
	US 2001-334654P	P	20011130
	WO 2002-EP1106	W	20020204
	US 2002-73845	A1	20020211

OTHER SOURCE(S): MARPAT 137:185502

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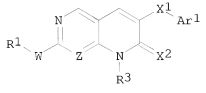

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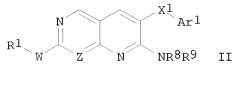

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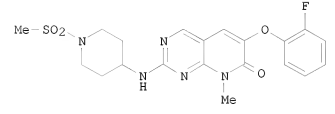


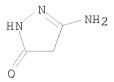
III

AB The title compds. with general formula I or II [wherein Z = N or CH; W = NR2; X1 = O, NR4, S, CR5R6, or CO; R4, R5, and R6 = independently H or alkyl; X2 = O or NR7; Ar1 = (hetero)aryl; R2 = H, alkyl, acyl, alkoxycarbonyl, aryloxycarbonyl, heteroalkyl(oxy)carbonyl, or R21-R22; R21 = alkylene or CO; R22 = alkyl or alkoxy; R1 = H, (halo)alkyl, (hetero)aryl, (hetero)aralkyl, cyclo(alkyl)alkyl, hetero(cyclyl)alkyl, cyanoalkyl, heterocyclyl, or substituted hetero(alkyl)cycloalkyl, heterocycloamino, or acyl(alkylene); R3 = H, (cyclo)alkyl, cycloalkylalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, acylalkylene, (un)substituted amino; R7 = H or alkyl; R8 and R9 = independently H, (cyclo)alkyl, aryl(sulfonyl), aralkyl, cycloalkylalkyl, heteroalkyl, alkylsulfonyl, acyl, etc.; and pharmaceutically acceptable salts thereof] were prepared For example, the substitution reaction of 6-(2-fluorophenoxy)-8-methyl-2-(methylsulfonyl)pyrido[2,3-d]pyrimidin-7(8H)-one (preparation given) and 1-(methylsulfonyl)piperidin-4-amine (preparation given), followed by salt formation, gave the phenoxypyrido[2,3-d]pyrimidinone III•HCl. I and II have IC50 activity against p38 kinase in the range of 0.1-5000 nM, with the majority being 1-1000 nM. I and II are useful for the treatment of arthritis, Crohn's disease, irritable bowel syndrome, adult respiratory distress syndrome, chronic obstructive pulmonary disease, or Alzheimer's disease (no data).

IT 6126-22-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of oxopyrido[2,3-d]pyrimidines for treating p38 mediated disorders)

RN 6126-22-3 CAPLUS

CN 3H-Pyrazol-3-one, 5-amino-2,4-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:637636 CAPLUS
DOCUMENT NUMBER: 137:185515
TITLE: Preparation of acylated indanyl amines and their use as remedies in upregulation of endothelial nitric oxide synthase
INVENTOR(S): Strobel, Hartmut; Wohlfart, Paulus; Safarova, Alena; Walser, Armin; Suzuki, Teri; Dharanipragada, Ramalinga M.
PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064545	A1	20020822	WO 2002-EP1444	20020212 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
TW 243164	B	20051111	TW 2002-91102295	20020208
CA 2437944	A1	20020822	CA 2002-2437944	20020212 <--
AU 2002253010	A1	20020828	AU 2002-253010	20020212 <--
AU 2002253010	B2	20080228		
AU 2002253010	B9	20080731		
EE 200300369	A	20031015	EE 2003-369	20020212 <--
EP 1373191	A1	20040102	EP 2002-722067	20020212
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BR 2002007211	A	20040127	BR 2002-7211	20020212
HU 2003003256	A2	20040128	HU 2003-3256	20020212
CN 1491207	A	20040421	CN 2002-804836	20020212
CN 1259307	C	20060614		
JP 2004518719	T	20040624	JP 2002-564478	20020212
NZ 527470	A	20050429	NZ 2002-527470	20020212
RU 2339614	C2	20081127	RU 2003-127682	20020212
US 20030055093	A1	20030320	US 2002-73160	20020213 <--
US 7179839	B2	20070220		
ZA 2003005413	A	20040428	ZA 2003-5413	20030714
MX 2003006974	A	20040402	MX 2003-6974	20030805
BG 108076	A	20050531	BG 2003-108076	20030807

IN 2003CN01252	A	20051118	IN 2003-CN1252		20030811
HK 1061015	A1	20061124	HK 2004-103976		20040603
US 20070082897	A1	20070412	US 2006-548501		20061011
PRIORITY APPLN. INFO.:			EP 2001-102850	A	20010213
			WO 2002-EP1444	W	20020212
			US 2002-73160	A3	20020213

OTHER SOURCE(S): MARPAT 137:185515

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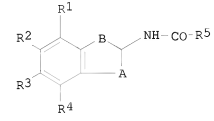

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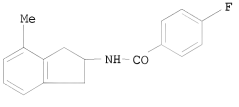


II

AB Title compds. [I; R1-R4 =; A = CH2, CHOH, CH(C1-C3-alkyl); B = CH2, CH(C1-C3-alkyl); R5 = aryl, heteroaryl] are prepared and are useful in the upregulation of endothelial nitric oxide synthase (eNOS). Title compds. I may therefore be useful for the manufacture of medicaments for the treatment of cardiovascular diseases, stable or unstable angina pectoris, coronary heart disease, Prinymetal angina, acute coronary syndrome, heart failure, myocardial infarction, stroke, thrombosis, peripheral artery occlusive disease, endothelial dysfunction, atherosclerosis, restenosis, endothelial damage after PTCA(percutaneous trans-luminal coronary angioplasty), hypertension, essential hypertension, pulmonary hypertension, secondary hypertension, renovascular hypertension, chronic glomerulonephritis, erectile dysfunction, ventricular arrhythmia, diabetes or diabetes complications, nephropathy or retinopathy, angiogenesis, asthma bronchial, chronic renal failure, cirrhosis of the liver, osteoporosis, restricted memory performance, a restricted ability to learn, or for the lowering of cardiovascular risk of postmenopausal women or after intake of contraceptives. Thus, the title compound II was prepared from 2-amino-4-methylindane and 4-fluorobenzoyl chloride, purified by HPLC and was in vitro tested on human umbilical vein cord endothelial cells for activation effect of eNOS transcription with EC-50(μM) = 6.0 and TIR(max) = 2.80.

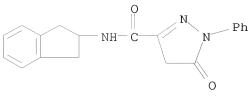
IT 450355-78-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation method of acylated indanyl amines and use as remedies in upregulation of endothelial nitric oxide synthase)

RN 450355-78-9 CAPLUS

CN 1H-Pyrazole-3-carboxamide, N-(2,3-dihydro-1H-inden-2-yl)-4,5-dihydro-5-oxo-1-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:916407 CAPLUS
DOCUMENT NUMBER: 136:53755
TITLE: Synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction
INVENTOR(S): Garvey, David S.; Saenz de Tejada, Inigo; Earl, Richard A.; Khanapure, Subhash P.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S., 117 pp., Cont.-in-part of U.S. 5,958,926. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 6331543	B1	20011218	US 1999-387727	19990901	<--
US 5874437	A	19990223	US 1996-740764	19961101	<--
WO 9819672	A1	19980514	WO 1997-US19870	19971031	<--
W: AU, CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 5958926	A	19990928	US 1998-145142	19980901	<--
US 20020019405	A1	20020214	US 2001-941691	20010830	<--
US 6462044	B2	20021008			
US 20030023087	A1	20030130	US 2002-216886	20020813	<--
US 6930113	B2	20050816			
US 20040087591	A1	20040506	US 2003-694183	20031028	
US 20080009498	A1	20080110	US 2007-819514	20070627	

PRIORITY APPLN. INFO.:
US 1996-740764 A2 19961101
WO 1997-US19870 A2 19971031
US 1998-145142 A2 19980901
US 1999-387727 A1 19990901
US 2001-941691 A3 20010830
US 2002-216866 A3 20020813
US 2002-216886 A3 20020813
US 2003-694183 B1 20031028

OTHER SOURCE(S): MARPAT 136:53755
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I-V, derivs. thereof, and certain substituted Ph and phthalzaine derivs. were claimed [D2 = H, alkyl, D; D = NO, NO2, alkyl, acyl, phosphoryl, silyl, etc.; A1-3 comprise the other subunits of a 5- or 6-membered monocyclic aromatic ring; R8 = H, (halo)alkyl; p = 1-10; R24 = H, cyclohexyl, piperidinyl, etc., with the proviso that at least one of A1-3,

J, or R24 contains T-Q or D; T = bond, O, S(O), amino; Q = NO, NO2; D1 = D or H; R37 = (hetero)aryl; R38 = H, halo, alkyl; G1 = alkyl, alkenyl or is part of a ring fused to the piperidine moiety of III; G4 = O, S; R40 = H, alkyl, haloalkyl, halo, etc.; R41 = alkyl, hydroxyalkyl, alkylcarboxy, etc.; R42 = aryl, alkylaryl, alkyloxyaryl; T1 = alkyl, oxyalkyl, thioalkyl, aminoalkyl]. Two synthetic examples were provided. E.g., the S-nitroso derivative of the 3-mercapto-3-methylbutyric acid ester of dipyridamole (VI) was prepared in 4 steps from dipyridamole in 3.5% overall yield. VI at doses of 10 and 30 μM was more efficacious in relaxing phenylephrine-induced tissue contraction than was the known phosphodiesterase inhibitor, dipyridamole. The present invention describes novel (nitrosated/nitrosylated) phosphodiesterase inhibitors, and compns. containing at least one (nitrosated/nitrosylated) phosphodiesterase inhibitor, and, optionally, one or more compds. that donate, transfer or release NO, elevate endogenous levels of endothelium-derived relaxing factor, stimulate endogenous synthesis of NO, or is a substrate for nitric oxide synthase and/or one or more vasoactive agents. The present invention also provides methods for treating or preventing sexual dysfunctions in males and females, for enhancing sexual responses in males and females, and for treating or preventing diseases induced by the increased metabolism of cGMP, such as hypertension, pulmonary hypertension, etc.

IT 137-44-0D, 2-Pyrazolin-5-one, nitroso derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction)

RN 137-44-0 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro- (CA INDEX NAME)

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:868447 CAPLUS
DOCUMENT NUMBER: 136:5917
TITLE: Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
INVENTOR(S): Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products Inc., USA
SOURCE: PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090101	A1	20011129	WO 2001-US13811	20010427 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 20030187020	A1	20031002	US 2001-843126	20010426	<--
US 6977263	B2	20051220			
CA 2409827	A1	20011129	CA 2001-2409827	20010427	<--
EP 1296972	A1	20030402	EP 2001-930925	20010427	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001011206	A	20030415	BR 2001-11206	20010427	<--
HU 2003002485	A2	20031229	HU 2003-2485	20010427	<--
HU 2003002485	A3	20070928			
JP 2004510697	T	20040408	JP 2001-586288	20010427	
CN 1230431	C	20051207	CN 2001-811952	20010427	
CN 1740169	A	20060301	CN 2005-10106304	20010427	
AU 2001257413	B2	20070118	AU 2001-257413	20010427	
MX 2002011400	A	20030523	MX 2002-11400	20021119	<--
IN 2002CN01892	A	20050211	IN 2002-CN1892	20021120	
ZA 2002009484	A	20040223	ZA 2002-9484	20021121	
KR 858642	B1	20080917	KR 2002-715683	20021121	
HK 1057899	A1	20060728	HK 2004-100765	20040206	
US 20050228018	A1	20051013	US 2005-57809	20050214	

PRIORITY APPLN. INFO.:	GB 2000-12362	A	20000522
	US 2001-843126	A	20010426
	CN 2001-811952	A3	20010427
	WO 2001-US13811	W	20010427

OTHER SOURCE(S): MARPAT 136:5917
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are β to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prepared Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester derivative of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf)•CH2Cl2, 80°C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temperature, 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temperature, 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

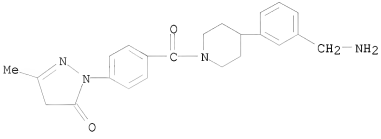
IT 375851-29-9P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors)

RN 375851-29-9 CAPLUS

CN 3H-Pyrazol-3-one, 2-[4-[[4-[3-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]phenyl]-2,4-dihydro-5-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 375851-28-8
CMF C23 H26 N4 O2



CM 2

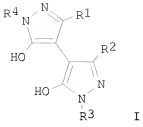
CRN 76-05-1
CMF C2 H F3 O2

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:742519 CAPLUS
DOCUMENT NUMBER: 130:38378
TITLE: Preparation of bipyrazole derivatives and pharmaceuticals or analytical reagents containing them
INVENTOR(S): Ohara, Heitaro; Igarashi, Takashi; Sakurai, Kazuhisa; Oshii, Tetsuo
PATENT ASSIGNEE(S): Daiichi Radioisotope Laboratories, Ltd., Japan; Yamagata Prefecture Technopolis Zaida
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10306077	A	19981117	JP 1997-131608	19970507 <--
PRIORITY APPLN. INFO.:			JP 1997-131608	19970507

OTHER SOURCE(S): MARPAT 130:38378
GI

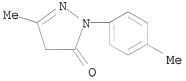


I

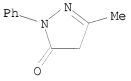
AB Pharmaceuticals for treatment of cerebral ischemia, heart diseases, gastrointestinal diseases, cancer, aging, inflammation , etc., due to reactive O species and free radicals or reagents for noninvasive ESR imaging and detection of free radicals in living tissues, contain bipyrazole derivs. I [R1, R2 = H, aryl, C1-5 alkyl, C3-6 alkoxycarbonylalkyl; R3, R4 = H, C1-5 alkyl, C5-7 cycloalkyl, C1-3 hydroxyalkyl, benzyl, naphthyl, (un)substituted phenyl] as active ingredients. Singlet oxygen generated in a photoexcited hematoporphyrin system was reacted with 5,5'-dihydroxy-3,3'-diphenyl-4,4'-bipyrazole to give ESR signal indicating production of stable free radical.

IT 86-92-0P 89-25-8P 89-36-1P 108-26-9P
876-92-6P 4845-49-2P 13024-90-3P
60798-06-3P 60875-16-3P 76858-78-1P
107430-36-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dihydroxybipyrazole derivs. as active O and free radical scavengers for pharmaceuticals and anal. reagents)

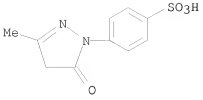
RN 86-92-0 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-(4-methylphenyl)- (CA INDEX NAME)



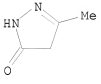
RN 89-25-8 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



RN 89-36-1 CAPLUS
CN Benzenesulfonic acid, 4-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)- (CA INDEX NAME)

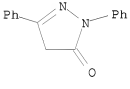


RN 108-26-9 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl- (CA INDEX NAME)

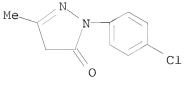


RN 876-92-6 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-phenyl- (CA INDEX NAME)

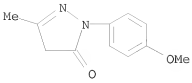
RN 4845-49-2 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2,5-diphenyl- (CA INDEX NAME)



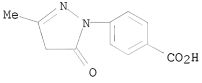
RN 13024-90-3 CAPLUS
CN 3H-Pyrazol-3-one, 2-(4-chlorophenyl)-2,4-dihydro-5-methyl- (CA INDEX NAME)



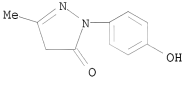
RN 60798-06-3 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-(4-methoxyphenyl)-5-methyl- (CA INDEX NAME)



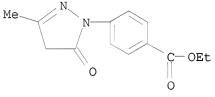
RN 60875-16-3 CAPLUS
CN Benzoic acid, 4-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)- (CA INDEX NAME)



RN 76858-78-1 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-(4-hydroxyphenyl)-5-methyl- (CA INDEX NAME)



RN 107430-36-4 CAPLUS
CN Benzoic acid, 4-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)-, ethyl ester (CA INDEX NAME)



L12 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:509066 CAPLUS
DOCUMENT NUMBER: 129:144878
ORIGINAL REFERENCE NO.: 129:29423a
TITLE: Pyrazole derivatives for cannabinoid receptor modulators, preparation, and therapeutic use
INVENTOR(S): Xiang, Jia Ning; Elliott, John Duncan; Atkinson, Steven Todd; Christensen, Siegfried Benjamin, IV
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831227	A1	19980723	WO 1998-US1175	19980120 <--
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2278307	A1	19980723	CA 1998-2278307	19980120 <--
EP 971588	A1	20000119	EP 1998-904629	19980120 <--
EP 971588	B1	20040317		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001508799	T	20010703	JP 1998-534688	19980120 <--
ES 2213892	T3	20040901	ES 1998-904629	19980120
US 6100259	A	20000808	US 1999-355151	19991015 <--

PRIORITY APPLN. INFO.: US 1997-35073P P 19970121
WO 1998-US1175 W 19980120

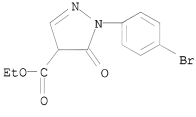
OTHER SOURCE(S): MARPAT 129:144878

AB Pyrazole derivs. are provided which are cannabinoid receptor modulators. The compds. of the invention may be used to treat a variety of diseases, e.g. immunol.-mediated inflammatory diseases and renal ischemia. Preparation of Et 5-(2-morpholin-4-ylethoxy)-1-[4-(2-formylphenyl)phenyl]pyrazole-4-carboxylate is described.

IT 66530-36-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; pyrazole derivs. for cannabinoid receptor modulators, preparation, and therapeutic use)

RN 66530-36-7 CAPLUS

CN 1H-Pyrazole-4-carboxylic acid, 1-(4-bromophenyl)-4,5-dihydro-5-oxo-, ethyl ester (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:616601 CAPLUS
DOCUMENT NUMBER: 125:275666
ORIGINAL REFERENCE NO.: 125:51553a,51556a
TITLE: Preparation of pyridyl-substituted sulfonamides as selective β3 adrenergic receptor agonists for the treatment of type II diabetes and obesity
INVENTOR(S): Fisher, Michael H.; Naylor, Elizabeth M.; Ok, Dong; Weber, Ann E.; Shih, Thomas; Ok, Hyun
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 35 pp., Cont.-in-part of U. S. Ser. No. 404,565, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent

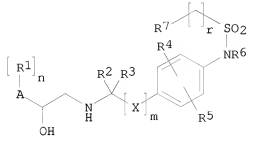
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5561142	A	19961001	US 1995-445630	19950522 <--
US 5705515	A	19980106	US 1996-684901	19960725 <--

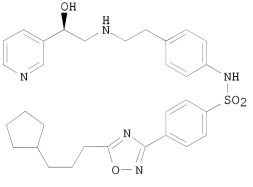
PRIORITY APPLN. INFO.:

US 1994-233166	B2	19940426
US 1995-404565	B2	19950321
US 1995-445630	A2	19950522

OTHER SOURCE(S): MARPAT 125:275666
GI



I



II

AB The title compds. [I; A = pyridinyl; R1 = OH, O, halo, etc.; R2, R3 = H, C1-10 alkyl, C1-10 alkoxy, etc.; X = CH2, (CH2)2, CH:CH, CH2O; R4, R5 = H, C1-10 alkyl, halo, etc.; R6 = H, C1-10 alkyl; R7 = (substituted) Ph, naphthyl, a 5- or 6-membered heterocyclic ring, etc.; n = 0-5; m = 0-1; r = 0-3], selective β3 adrenergic receptor agonists and therefore useful in the treatment of type II diabetes and obesity as well as neurogenic inflammation, depression, gastrointestinal disorders, gut motility and as lowering triglyceride and cholesterol levels agents, were prepared by coupling an aminoalkylphenylsulfonamide with an appropriately substituted epoxide. Thus, refluxing (R)-(pyrid-3-yl)oxirane with N-[4-(2-aminoethyl)phenyl]-4-[5-(3-cyclopentylpropyl)[1,2,4]-oxadiazol-3-yl]benzenesulfonamide in dry MeOH afforded the desired product (R)-II. Compds. I were effective at 0.07-350 mg/day when treating diabetes mellitus and/or hyperglycemia.

IT 173902-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridyl-substituted sulfonamides as selective β3

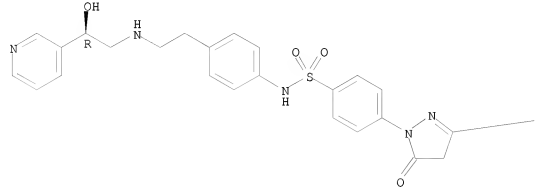
adrenergic receptor agonists for the treatment of type II diabetes and obesity)

RN 173902-20-0 CAPLUS

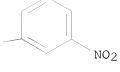
CN Benzenesulfonamide, 4-[4,5-dihydro-3-(3-nitrophenyl)-5-oxo-1H-pyrazol-1-yl]-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 182251-93-0P

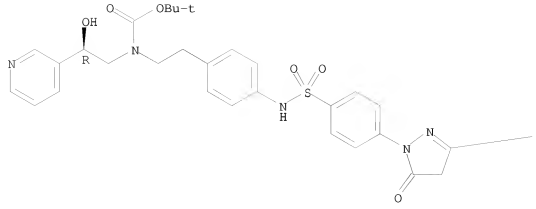
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

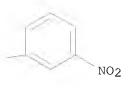
(preparation of pyridyl-substituted sulfonamides as selective β3 adrenergic receptor agonists for the treatment of type II diabetes and obesity)

RN 182251-93-0 CAPLUS

CN Carbamic acid, [2-[4-[[[4-[4,5-dihydro-3-(3-nitrophenyl)-5-oxo-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]phenyl]ethyl][2-hydroxy-2-(3-pyridinyl)ethyl]-, 1,1-dimethylethyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:494735 CAPLUS
DOCUMENT NUMBER: 125:221588
ORIGINAL REFERENCE NO.: 125:41417a,41420a
TITLE: Substituted sulfonamides as selective β3 agonists for the treatment of diabetes and obesity
INVENTOR(S): Fisher, Michael H.; Naylor, Elizabeth M.; Weber, Ann E.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 233,166,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5541197	A	19960730	US 1995-404566	19950321 <--
IL 113410	A	19991130	IL 1995-113410	19950418 <--
CA 2187932	A1	19951102	CA 1995-2187932	19950421 <--
WO 9529159	A1	19951102	WO 1995-US4956	19950421 <--

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9523937	A	19951116	AU 1995-23937	19950421	<--
AU 687558	B2	19980226			
EP 757674	A1	19970212	EP 1995-917116	19950421	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
CN 1149869	A	19970514	CN 1995-192821	19950421	<--
HU 76442	A2	19970929	HU 1996-2951	19950421	<--
JP 09512275	T	19971209	JP 1995-527797	19950421	<--
JP 3149186	B2	20010326			
ZA 9503336	A	19960109	ZA 1995-3336	19950425	<--
FI 9604314	A	19961025	FI 1996-4314	19961025	<--

PRIORITY APPLN. INFO.:	US 1994-233166	B2	19940426
	US 1995-404565	A	19950321
	US 1995-404566	A	19950321
	WO 1995-US4956	W	19950421

OTHER SOURCE(S): MARPAT 125:221588
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Substituted sulfonamides I wherein: n is 0-5; m is 0 or 1; p is 0-3; ring A is (1) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (2) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (3) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (4) Ph, or (5) a benzene ring fused to a C3-8 cycloalkyl ring; R1 is, e.g., OH, oxo, halo; R2 and R3 are independently (1) hydrogen, (2) C1-C10 alkyl or (3) C1-C10 alkyl with 1 to 4 substituents selected from hydroxy, C1-C10 alkoxy, and halogen; X is(1) CH2, (2) CH2CH2, (3) CH:CH, or (4) CH2O; R4 and R5 are independently , e.g., hydrogen, C1-C10 alkyl, halogen; R6 is (1) hydrogen or (2) C1-C10 alkyl; R7 is Z-(R1a)n; R1a is, e.g., R1 (with proviso), C3-8 cycloalkyl, optionally substituted Ph; Z is, e.g., Ph, naphthyl, heterocyclic, are selective β3 adrenergic receptor agonists with very little β1 and β2 adrenergic receptor activity and as such the compds. are capable of increasing lipolysis and energy expenditure in cells (no data). The compds. thus have potent activity in the treatment of Type II diabetes and obesity. The compds. can also be used to lower triglyceride levels and cholesterol levels or raise high d. lipoprotein levels or to decrease gut motility. In addition, the compds. can be used to reduced neurogenic inflammation or as antidepressant agents. Compns. and methods for the use of the compds. in the treatment of diabetes and obesity and for lowering triglyceride levels and cholesterol levels or raising high d. lipoprotein levels or for increasing gut motility are also disclosed. Thus, e.g., ring cleavage of (R)-2-(tetrazolo[1,5-a]pyrid-6-yl)oxirane with 2-(4-aminophenyl)ethylamine followed by Boc protection afforded amino alc. II; chlorosulfonylation of N-hexyl-N'-phenylurea (from hexylamine + Ph isocyanate) provided N-hexyl-N'-(4-chlorosulfonylphenyl)urea III; coupling of II + III followed by deprotection afforded sulfonamide IV.

IT 173902-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

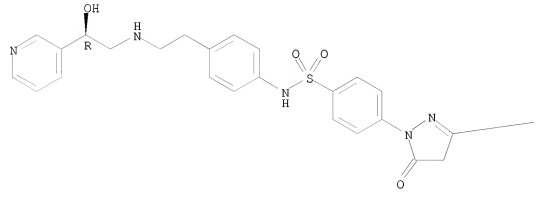
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted sulfonamides as selective β3 agonists for the treatment of diabetes and obesity)

RN 173902-20-0 CAPLUS

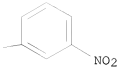
CN Benzenesulfonamide, 4-[4,5-dihydro-3-(3-nitrophenyl)-5-oxo-1H-pyrazol-1-yl]-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

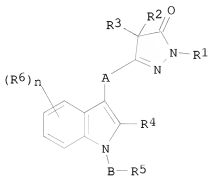
L12 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1996:106719 CAPLUS
DOCUMENT NUMBER:	124:289527
ORIGINAL REFERENCE NO.:	124:53694h,53695a
TITLE:	Substituted 3-indolyl-5-pyrazolone compounds as UV-absorbing additives in plastic compositions and as inflammation and β-amyloid peptide inhibitors
INVENTOR(S):	Grant, Francine S.; Fang, Lawrence Y.; John, Varghese; Thorsett, Eugene D.
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S., 24 pp. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5484940	A	19960116	US 1994-345973	19941128 <--
PRIORITY APPLN. INFO.:			US 1994-345973	19941128

OTHER SOURCE(S): MARPAT 124:289527
GI



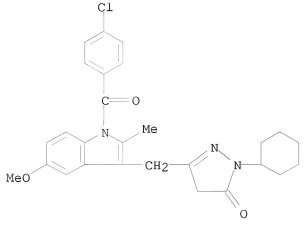
I

AB This invention is directed to novel substituted 3-indolyl-5-pyrazolone compds. I wherein: R1 = H, alkyl of from 1 to 10 carbon atoms optionally substituted, cycloalkyl, aryl, heterocyclyl; R2 and R3 are independently H, alkyl of from 1 to 10 carbon atoms, or R2R3 together define :CR13R14 where R13 and R14 are independently H, alkyl of from 1 to 10 carbon atoms, Ph; R4 = H, alkyl of from 1 to 10 carbon atoms, R5 = H, alkyl of from 1 to 10 carbon atoms optionally substituted, aryl; each R6 is independently, e.g., halo, nitro, cyano; n is an integer from 0 to 3; A = XR9 where X is selected from the group consisting of a bond, O and S(O)p where p is an integer of from 0 to 2 and R9 is an alkylene group of from 1 to 6 carbon atoms; and B = e.g., a bond, an alkylene group of from 1 to 6 carbon atoms, with the proviso that when R2 and/or R3 is hydrogen, the compds. of formula I above can exist in the enol tautomeric form, which can absorb UV light and, accordingly, are useful as additives in plastic comps. and the like where absorption of UV light is an important requirement of the composition Addnl., the compds. described herein possess anti-inflammatory properties and some of the compds. also are able to inhibit both in vivo and in vitro the generation of β-amyloid peptide in, for example, a cultured cell medium as well as inhibit the toxicity of the β-amyloid peptide toward human neuronal cells; thus, the compds. are useful both prophylactically and therapeutically in the prevention and treatment of Alzheimer's disease. Thus, e.g., 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-3-indoleacetic acid was converted to an active ester and treated with Et hydrogen malonate Mg enolate to afford Et 4-[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-3-indolyl]-3-oxobutyrate; heterocyclization of the latter with phenylhydrazine hydrochloride afforded 3-[1-(4-clorobenzoyl)-5-methoxy-2-methyl-3-indolylmethyl]-1-phenyl-5-pyrazolone which reduced β-amyloid peptide production by at least 20% as compared to control, and inhibited by at least 25% the toxicity of β-amyloid to human neuronal cells. Similarly prepared was 3-[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylmethyl]-1-cyclohexyl-5-pyrazolone which possessed λmax = 251 nm, extinction coefficient = 23.29 au/mg/mL/cm, and which exhibited 75% inhibition of 5-lipoxygenase at 6μM. Pharmaceutical formulations were given.

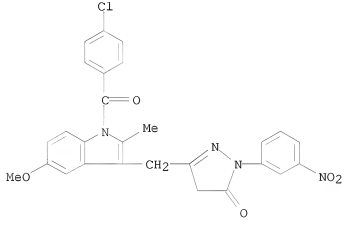
IT 175459-22-0P 175459-43-5P 175459-53-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); MOA (Modifier or additive use); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(substituted 3-indolyl-5-pyrazolone compds. as UV-absorbing additives in plastic compns. and as inflammation and β-amyloid peptide inhibitors)

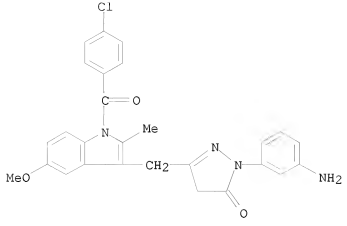
RN 175459-22-0 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-cyclohexyl-2,4-dihydro- (CA INDEX NAME)



RN 175459-43-5 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-(3-nitrophenyl)- (CA INDEX NAME)



RN 175459-53-7 CAPLUS
CN 3H-Pyrazol-3-one, 2-(3-aminophenyl)-5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro- (CA INDEX NAME)



IT 175459-14-0P 175459-21-9P 175459-23-1P
175459-24-2P 175459-25-3P 175459-28-6P
175459-30-0P 175459-31-1P 175459-32-2P
175459-33-3P 175459-34-4P 175459-35-5P
175459-36-6P 175459-37-7P 175459-38-8P
175459-39-9P 175459-40-2P 175459-41-3P
175459-42-4P 175459-44-6P 175459-45-7P
175459-46-8P 175459-47-9P 175459-50-4P
175459-52-6P 175459-54-8P 175459-56-0P
175459-60-6P 175459-62-8P 175459-64-0P
175459-66-2P 175459-68-4P 175459-70-8P
175459-71-9P 175459-73-1P 175459-75-3P
175459-76-4P 175459-78-6P 175459-79-7P
175459-83-3P 175459-84-4P 175459-85-5P
175459-86-6P 175459-87-7P 175459-88-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MOA (Modifier or additive use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted 3-indolyl-5-pyrazolone compds. as UV-absorbing additives in plastic compns. and as inflammation and β-amyloid peptide inhibitors)

RN 175459-14-0 CAPLUS

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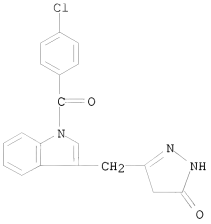
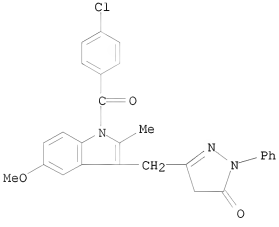
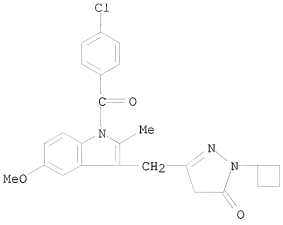


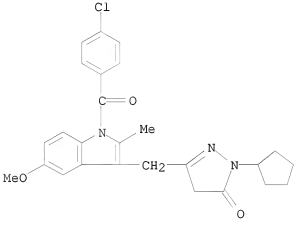
RN 175459-21-9 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-phenyl- (CA INDEX NAME)



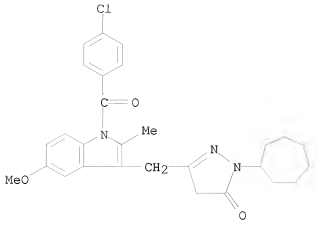
RN 175459-23-1 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-cyclobutyl-2,4-dihydro- (CA INDEX NAME)



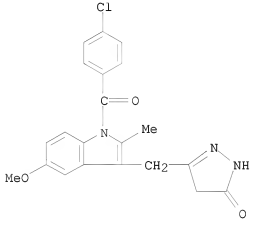
RN 175459-24-2 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-cyclopentyl-2,4-dihydro- (CA INDEX NAME)



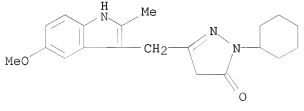
RN 175459-25-3 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-cycloheptyl-2,4-dihydro- (CA INDEX NAME)



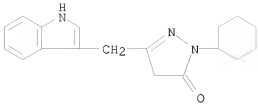
RN 175459-28-6 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro- (CA INDEX NAME)



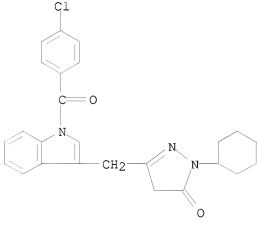
RN 175459-30-0 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[(5-methoxy-2-methyl-1H-indol-3-yl)methyl]- (CA INDEX NAME)



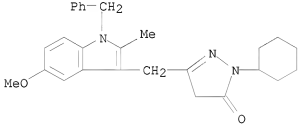
RN 175459-31-1 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-(1H-indol-3-ylmethyl)- (CA INDEX NAME)



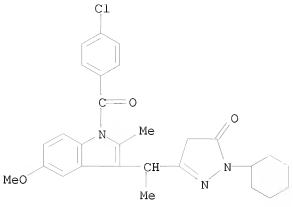
RN 175459-32-2 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-1H-indol-3-yl]methyl]-2-cyclohexyl-2,4-dihydro- (CA INDEX NAME)



RN 175459-33-3 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[[5-methoxy-2-methyl-1-(phenylmethyl)-1H-indol-3-yl]methyl]- (CA INDEX NAME)



RN 175459-34-4 CAPLUS
CN 3H-Pyrazol-3-one, 5-[1-[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]ethyl]-2-cyclohexyl-2,4-dihydro- (CA INDEX NAME)



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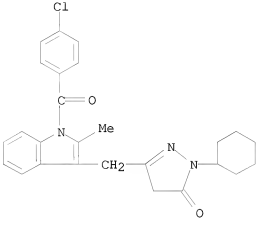

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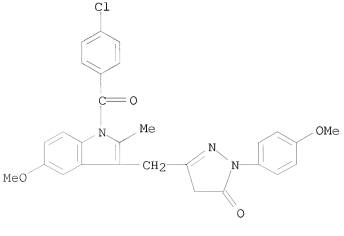
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-(4-methoxyphenyl)- (CA INDEX NAME)



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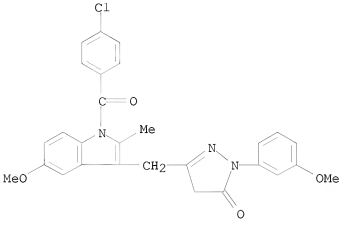
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-(3-methoxyphenyl)- (CA INDEX NAME)



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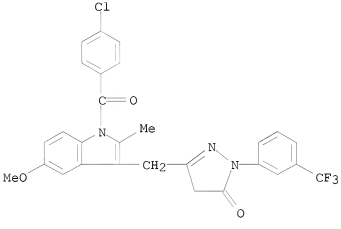
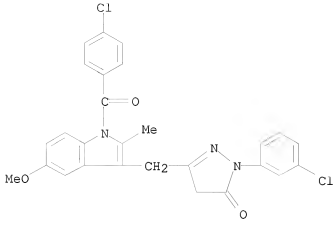
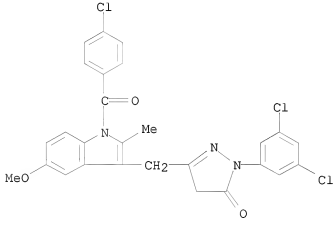
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 175459-39-9 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-(3-chlorophenyl)-2,4-dihydro- (CA INDEX NAME)



RN 175459-40-2 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-(3,5-dichlorophenyl)-2,4-dihydro- (CA INDEX NAME)



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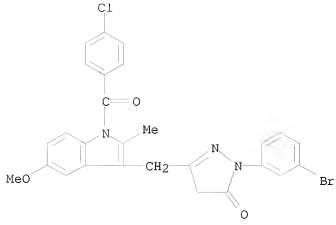
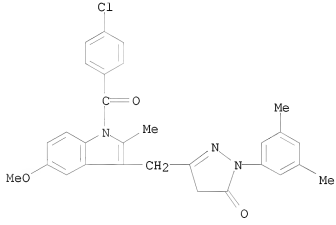
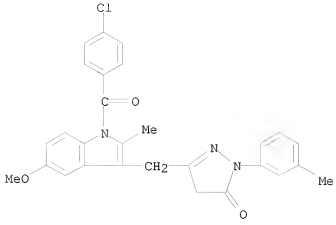
CN 3H-Pyrazol-3-one, 2-(3-bromophenyl)-5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro- (CA INDEX NAME)



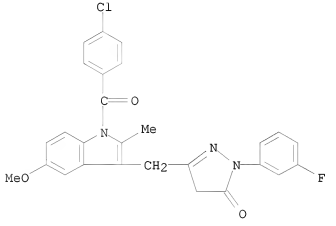
RN 175459-42-4 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-(3,5-dimethylphenyl)-2,4-dihydro- (CA INDEX NAME)



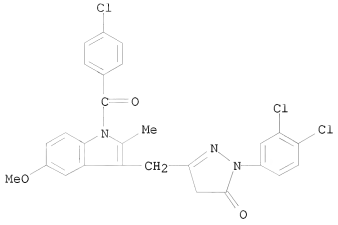
RN 175459-44-6 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-(3-methylphenyl)- (CA INDEX NAME)



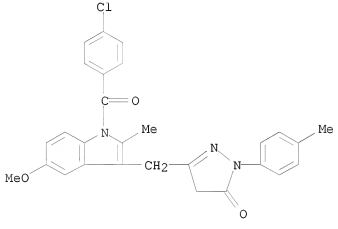
RN 175459-45-7 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-(3-fluorophenyl)-2,4-dihydro- (CA INDEX NAME)



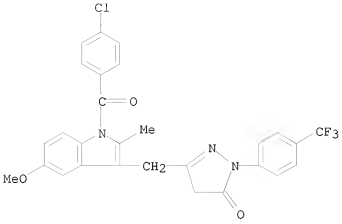
RN 175459-46-8 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-(3,4-dichlorophenyl)-2,4-dihydro- (CA INDEX NAME)



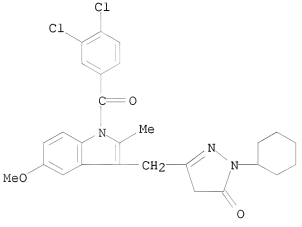
RN 175459-47-9 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-(4-methylphenyl)- (CA INDEX NAME)



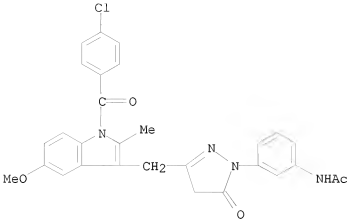
RN 175459-50-4 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)



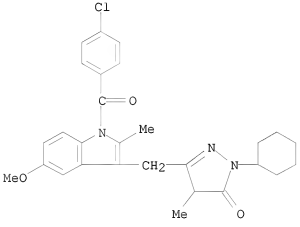
RN 175459-52-6 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-5-[[1-(3,4-dichlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro- (CA INDEX NAME)



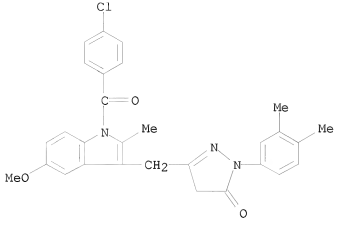
RN 175459-54-8 CAPLUS
CN Acetamide, N-[3-[3-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-4,5-dihydro-5-oxo-1H-pyrazol-1-yl]phenyl]- (CA INDEX NAME)



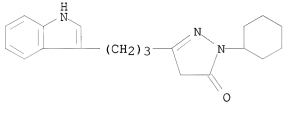
RN 175459-56-0 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-cyclohexyl-2,4-dihydro-4-methyl- (CA INDEX NAME)



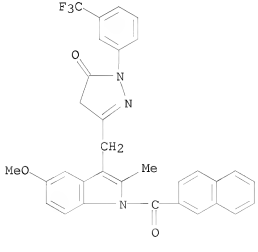
RN 175459-60-6 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2-(3,4-dimethylphenyl)-2,4-dihydro- (CA INDEX NAME)



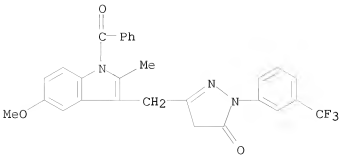
RN 175459-62-8 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[3-(1H-indol-3-yl)propyl]-
(CA INDEX NAME)



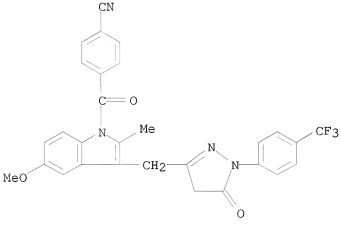
RN 175459-64-0 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-[[5-methoxy-2-methyl-1-(2-
naphthalenylcarbonyl)-1H-indol-3-yl]methyl]-2-[3-(trifluoromethyl)phenyl]-
(CA INDEX NAME)



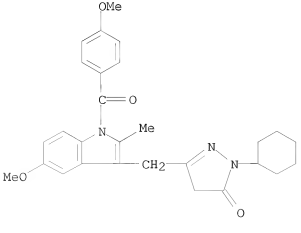
RN 175459-66-2 CAPLUS
CN 3H-Pyrazol-3-one, 5-[(1-benzoyl-5-methoxy-2-methyl-1H-indol-3-yl)methyl]-
2,4-dihydro-2-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 175459-68-4 CAPLUS
CN Benzonitrile, 4-[[3-[[4,5-dihydro-5-oxo-1-[4-(trifluoromethyl)phenyl]-1H-pyrazol-3-yl]methyl]-5-methoxy-2-methyl-1H-indol-1-yl]carbonyl]- (CA INDEX NAME)

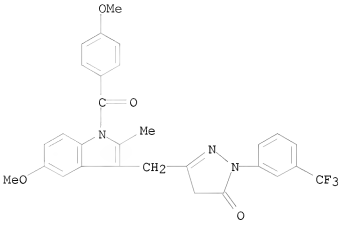


RN 175459-70-8 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[[5-methoxy-1-(4-methoxybenzoyl)-2-methyl-1H-indol-3-yl]methyl]- (CA INDEX NAME)

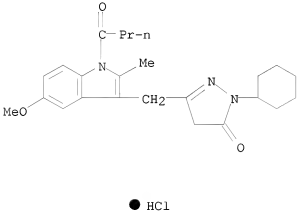


RN 175459-71-9 CAPLUS

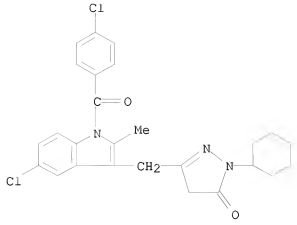
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-[[5-methoxy-1-(4-methoxybenzoyl)-2-methyl-1H-indol-3-yl]methyl]-2-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 175459-73-1 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[[5-methoxy-2-methyl-1-(1-oxobutyl)-1H-indol-3-yl]methyl]-, hydrochloride (1:1) (CA INDEX NAME)

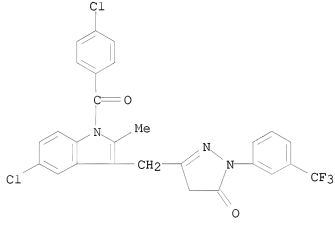


RN 175459-75-3 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[5-chloro-1-(4-chlorobenzoyl)-2-methyl-1H-indol-3-yl]methyl]-2-cyclohexyl-2,4-dihydro-, hydrochloride (1:1) (CA INDEX NAME)

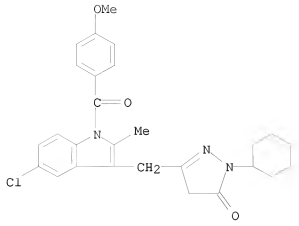


● HCl

RN 175459-76-4 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[5-chloro-1-(4-chlorobenzoyl)-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

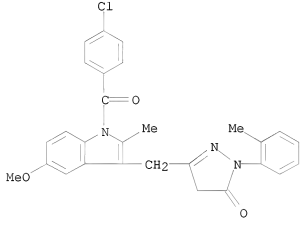


RN 175459-78-6 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[5-chloro-1-(4-methoxybenzoyl)-2-methyl-1H-indol-3-yl]methyl]-2-cyclohexyl-2,4-dihydro-, hydrochloride (1:1) (CA INDEX NAME)

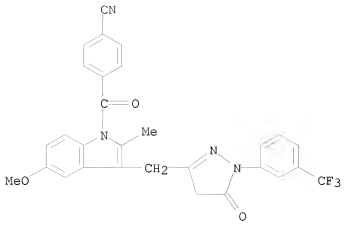


● HCl

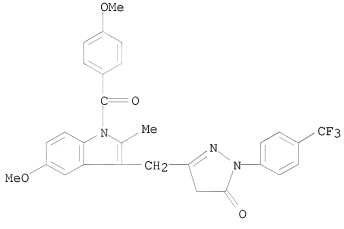
RN 175459-79-7 CAPLUS
CN 3H-Pyrazol-3-one, 5-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]methyl]-2,4-dihydro-2-(2-methylphenyl)- (CA INDEX NAME)



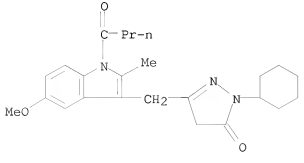
RN 175459-83-3 CAPLUS
CN Benzonitrile, 4-[[3-[[4,5-dihydro-5-oxo-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-3-yl]methyl]-5-methoxy-2-methyl-1H-indol-1-yl]carbonyl]- (CA INDEX NAME)



RN 175459-84-4 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-[[5-methoxy-1-(4-methoxybenzoyl)-2-methyl-1H-indol-3-yl]methyl]-2-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)

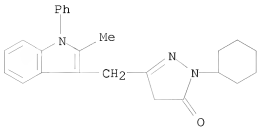


RN 175459-85-5 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[[5-methoxy-2-methyl-1-(1-oxobutyl)-1H-indol-3-yl]methyl]- (CA INDEX NAME)

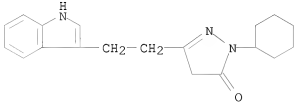


RN 175459-86-6 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[(2-methyl-1-phenyl-1H-indol-

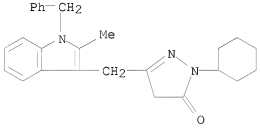
3-yl)methyl]- (CA INDEX NAME)



RN 175459-87-7 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[2-(1H-indol-3-yl)ethyl]-
(CA INDEX NAME)



RN 175459-88-8 CAPLUS
CN 3H-Pyrazol-3-one, 2-cyclohexyl-2,4-dihydro-5-[[2-methyl-1-(phenylmethyl)-
1H-indol-3-yl]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

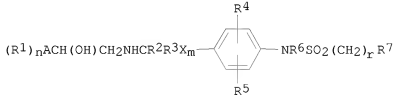
L12 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:998182 CAPLUS
DOCUMENT NUMBER: 124:176115
ORIGINAL REFERENCE NO.: 124:32663a,32666a
TITLE: Preparation of substituted arylsulfonamides as selective β3 agonists for the treatment of diabetes and obesity.
INVENTOR(S): Fisher, Michael H.; Naylor, Elisabeth M.; Ok, Dong; Weber, Ann E.; Shih, Thomas; Ok, Hyun
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9529159	A1	19951102	WO 1995-US4956	19950421 <--
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5541197	A	19960730	US 1995-404566	19950321 <--
AU 9523937	A	19951116	AU 1995-23937	19950421 <--
AU 687558	B2	19980226		
EP 757674	A1	19970212	EP 1995-917116	19950421 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09512275	T	19971209	JP 1995-527797	19950421 <--
JP 3149186	B2	20010326		
FI 9604314	A	19961025	FI 1996-4314	19961025 <--
PRIORITY APPLN. INFO.:			US 1994-233166 A	19940426
			US 1995-404565 A	19950321
			US 1995-404566 A	19950321
			WO 1995-US4956 W	19950421

OTHER SOURCE(S): MARPAT 124:176115

GI



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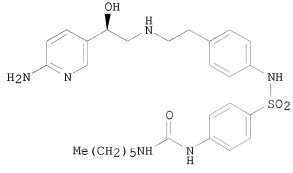


II

AB Title compds. [I; m = 0, 1; n = 0-5; r = 0-3; A = heterocyclyl, benzoheterocyclyl, heterocycloheterocyclyl, Ph, benzocycloalkyl; R1 = OH, O, halo, cyano, amino, CF3, sulfonylamino, (substituted) alkyl, etc.; R2, R3 = H, (substituted) alkyl; R4, R5 = H, alkyl, halo, amino, sulfonylamino, OH, etc; R6 = H, alkyl; R7 = Z(R11)n; R11 = R1, provided that when A = Ph, R11 ≠ alkyl; X = CH2, CH2CH2, CH:CH, CH2O; Z = Ph, naphthyl, heterocyclyl, heterocycloheterocyclyl] were prepared as selective β3 adrenergic receptor agonists with very little β1 and β2 adrenergic receptor activity which are capable of increasing lipolysis and energy expenditure in cells (no data). The compds. thus have potent

activity in the treatment of Type II diabetes and obesity. The compds. can also be used to lower triglyceride levels and cholesterol levels or raise high d. lipoprotein levels or to decrease gut motility. In addition, the compds. can be used to reduce neurogenic inflammation or as antidepressant agents. Title compound (II) was prepared in several steps.

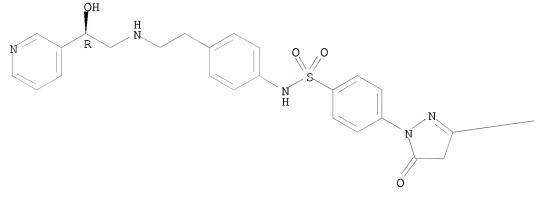
IT 173902-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted sulfonamides as selective β3 agonists for the treatment of diabetes and obesity)

RN 173902-20-0 CAPLUS

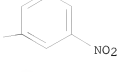
CN Benzenesulfonamide, 4-[4,5-dihydro-3-(3-nitrophenyl)-5-oxo-1H-pyrazol-1-yl]-N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

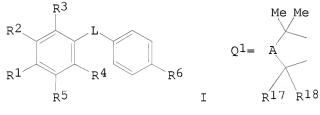
L12 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:42807 CAPLUS
DOCUMENT NUMBER: 114:42807
ORIGINAL REFERENCE NO.: 114:7457a,7460a
TITLE: Preparation of diarylheterocycles as drugs and cosmetics
INVENTOR(S): Wuest, Hans Heiner; Janssen, Bernd

PATENT ASSIGNEE(S): BASF A.-G., Germany
SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

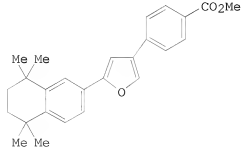
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3903993	A1	19900816	DE 1989-3903993	19890210 <--
EP 382077	A2	19900816	EP 1990-101947	19900201 <--
EP 382077	A3	19910731		
EP 382077	B1	19950517		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
CA 2009604	A1	19900810	CA 1990-2009604	19900208 <--
CA 2009604	C	20010102		
US 5061705	A	19911029	US 1990-476875	19900208 <--
JP 02240058	A	19900925	JP 1990-28617	19900209 <--
JP 2930645	B2	19990803		
US 5196532	A	19930323	US 1991-717264	19910618 <--
US 5206242	A	19930427	US 1991-753916	19910903 <--
US 5338749	A	19940816	US 1992-972518	19921106 <--
US 5475017	A	19951212	US 1994-242415	19940513 <--

PRIORITY APPLN. INFO.:
DE 1989-3903993 A 19890210
US 1990-476875 A3 19900208
US 1991-717264 A3 19910618
US 1992-972518 A3 19921106

OTHER SOURCE(S): CASREACT 114:42807; MARPAT 114:42807
GI



I



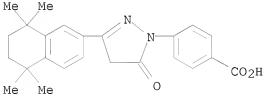
II

AB The title compds. [I; R1 = H, OH, R2 = Me3C; R1R2 = Q1; A = (Me-, HO-, or O-substituted) CH2, CH2CH2; L = (HO-, HS-, alkyl-, or alkanoyl-substituted) heterocyclyl; R3 = H, OH, alkoxy; R4 = H, alkyl, halo, MeO; R5 = H, MeO, Me3C; R6 = H, Me, cyano, alkylthio, alkylsulfinyl, alkylsulfonyl, hydroxymethyl, etc.; R17, R18 = H, Me] were prepared as drugs and cosmetics (no data). Thus, 6-acetyl-1,2,3,4-tetrahydro-1,1,4,4-

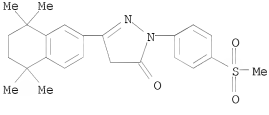
tetramethylnaphthalene and 4-HCOC6H4CO2Me were stirred 16 h in MeOH containing NaOH to give 3-(4-carbomethoxyphenyl)-1-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-2-propen-1-one. The latter was stirred with MeNO2 and Triton B in MeOH to give a residue which in CH2Cl2/THF at -25° was treated with NaOMe in MeOH. The resulting solution was added to a -25° solution of H2SO4 in MeOH to give 3-(4-carbomethoxyphenyl)-4-dimethoxy-1-(5,5,8,8-tetramethyl-2-naphthalenyl)-1-butanone. The latter was stirred 12 h in concentrated H2SO4 at 25° to give furan-containing title compound II. I are claimed to be useful against skin disorders, precancerous lesions, tumors, rheumatic and arthritic disease, dry eye, etc.

IT 131331-39-0P 131331-78-7P 131331-79-8P
131331-80-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as drug and cosmetic)

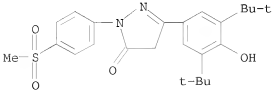
RN 131331-39-0 CAPLUS
CN Benzoic acid, 4-[4,5-dihydro-5-oxo-3-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-1H-pyrazol-1-yl]- (CA INDEX NAME)



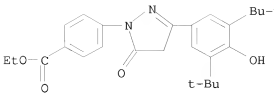
RN 131331-78-7 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-[4-(methylsulfonyl)phenyl]-5-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)- (CA INDEX NAME)



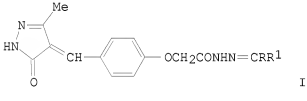
RN 131331-79-8 CAPLUS
CN 3H-Pyrazol-3-one, 5-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2,4-dihydro-2-[4-(methylsulfonyl)phenyl]- (CA INDEX NAME)



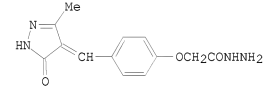
RN 131331-80-1 CAPLUS
CN Benzoic acid, 4-[3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-4,5-dihydro-5-oxo-1H-pyrazol-1-yl]-, ethyl ester (CA INDEX NAME)



L12 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1987:102148 CAPLUS
DOCUMENT NUMBER: 106:102148
ORIGINAL REFERENCE NO.: 106:16731a,16734a
TITLE: Synthesis of some newer 4-(3-methyl-5-oxo-4-pyrazolidinylidenemethyl)phenoxyacetic acid benzylidenehydrazides and α-methylbenzylidenehydrazides as CNS active and antiinflammatory agents
AUTHOR(S): Mohan, Rajiv Ravindra; Agarwal, Chapla; Misra, V. S.
CORPORATE SOURCE: Dep. Chem., Univ. Lucknow, Lucknow, 226 007, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1986), 25B(3), 339-41
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:102148
GI



I



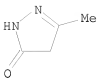
II

AB The title compds. I (R = H, Me; R1 = Ph, substituted phenyl) were prepared by condensation of hydrazides II with RCOR2. II was prepared by condensation of 3-methyl-5-oxopyrazole with p-OHCC6H4OCH2CO2Et followed by treatment with H2NNH2.H2O. I had central nervous systems stimulant or depressant activity and gave 4-23% protection against carrageenin-induced mice paw edema.

IT 108-26-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with Et fomrylphenoxyacetate)

RN 108-26-9 CAPLUS

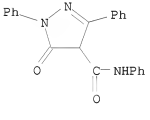
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl- (CA INDEX NAME)



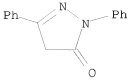
L12 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1975:593308 CAPLUS
DOCUMENT NUMBER: 83:193308
ORIGINAL REFERENCE NO.: 83:30413a,30416a
TITLE: 3-Aryl-5-oxo-2-pyrazoline-4-carboxanilides
INVENTOR(S): Zinnes, Harold; Lindo, Neil A.
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3905997	A	19750916	US 1974-481925	19740621 <--

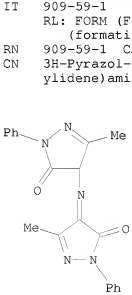
PRIORITY APPLN. INFO.: US 1974-481925 19740621
GI For diagram(s), see printed CA Issue.
AB Pyrazolinecarboxanilides (I; R = CONHPh; R1 = Me, Ph), with antiinflammatory activity in rats and useful in rheumatoid arthritis treatment, were prepared by treating I (R = H) with NaH in THF or DMF and then with PhNCO.
IT 57247-48-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 57247-48-0 CAPLUS
CN 1H-Pyrazole-4-carboxamide, 4,5-dihydro-5-oxo-N,1,3-triphenyl- (CA INDEX NAME)



IT 4845-49-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with sodium hydride and phenyl isocyanate)
RN 4845-49-2 CAPLUS
CN 3H-Pyrazol-3-one, 2,4-dihydro-2,5-diphenyl- (CA INDEX NAME)



L12 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1971:97665 CAPLUS
DOCUMENT NUMBER: 74:97665
ORIGINAL REFERENCE NO.: 74:15883a,15886a
TITLE: Biopharmaceutical studies on 4-(aminoethanesulfonylamino)antipyrine and related compounds. I
AUTHOR(S): Naito, Shunichi; Ueno, Yasuko; Yamaguchi, Hisashi; Nakai, Toshio
CORPORATE SOURCE: Kyoto Coll. Pharm., Kyoto, Japan
SOURCE: Journal of Pharmaceutical Sciences (1971), 60(2), 245-9
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB In rabbits, taurinopyrine (4-(aminoethanesulfonyl-amino)antipyrine) (I) (300 mg/kg, orally) produced a peak blood level of 81.3 μg/ml 2 hr after administration; 82% of this amount was bound to serum proteins. The binding of I with rabbit serum in vitro amounted to about 85%. Following ingestion of 400 mg I/kg, rubazonic acid (trace), 4-hydroxyantipyrine (trace), 4-acetylaminoantipyrine (4.37%), 4-aminoantipyrine (8%), and unchanged I (48.3%) were excreted in the urine. Hydrolysis of the glucuronides excreted in the urine following I treatment yielded 4-hydroxyantipyrine and 4-aminoantipyrine. I showed analgesic, antiinflammatory, antihistaminic, and antipyretic activities.
IT 909-59-1
RL: FORM (Formation, nonpreparative)
(formation of, from taurinopyrine)
RN 909-59-1 CAPLUS
CN 3H-Pyrazol-3-one, 4-[(1,5-dihydro-3-methyl-5-oxo-1-phenyl-4H-pyrazol-4-ylidene)amino]-2,4-dihydro-5-methyl-2-phenyl- (CA INDEX NAME)



L12 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:51905 CAPLUS
DOCUMENT NUMBER: 64:51905

ORIGINAL REFERENCE NO.: 64:9677f-h,9678a-d
TITLE: Reactions of hydrazine derivatives. XLIII. Addition of hydrazines to vinylpyridines
AUTHOR(S): Suminov, S. I.; Kost, A. N.
CORPORATE SOURCE: State Univ., Moscow
SOURCE: Zhurnal Organicheskoi Khimii (1965), 1(11), 2055-61
CODEN: ZORKAE; ISSN: 0514-7492
DOCUMENT TYPE: Journal
LANGUAGE: Russian

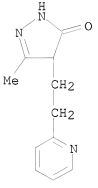
AB cf. CA 63, 6804d; 64, 584g. N2H4. H2O and 2-vinylpyridine in the presence of a small amount of N2H4. HCl gave after refluxing 1 hr. 78% 2-(2-hydrazinoethyl)pyridine (Ia), b7 135-6°, dipicrate, m. 146°; tartrate monohydrate, m. 128.5-9.5°. The following were less effective catalysts: AcOH, N2H4. H2SO4, BuOH; without a catalyst the yield was 31% while H2O, dioxane, Et3N and EtCN gave very low yields. In a similar reaction in refluxing MeOH, AcOH was the most effective catalyst, while N2H4. H2SO4 and N2H4. HCl were somewhat less effective. 4-Vinylpyridine heated 2 hrs. with N2H4. H2O gave 88% 4-(2-hydrazinoethyl)pyridine (I), b2 142-4°, n20D 1.5553; similar reaction with AcOH as catalyst gave a similar yield; N2H4. HCl was ineffective; the product gave HCl salt, m. 149-9.5°; dipicrate, m. 162°; monophenylthioureide, m. 135-5.5°; p-nitrobenzylidene derivative, m. 137.5-38°; N,N'-dibenzoyl derivative, m. 149-50°. I and AcCH2CO2Et mixed in C6H6 at below 60° and kept overnight gave 89% 3-methyl-1-[2-(4-pyridyl)ethyl]-5-pyrazolone, m. 145-6°; similarly prepared was 100% 3-phenyl analog, m. 140-40.5°. AcCH2CO2Et subjected to 2-pyridylethylation (Boekelheide and Rothchild, CA 43, 4267e) and treated with 80% N2H4. H2O at 105° 0.5 hr. gave 3-methyl-4-[2-(2-pyridyl)ethyl]-5-pyrazolone m. 214°. Ia and 2-vinylpyridine heated at 110° in the presence of AcOH gave bis(py-ridylethyl)hydrazines, b6 200-5°, which gave a tri-HCl salt, m. 162-3.5°, identified as that of bis[(2-(2-pyridyl)ethyl]hydrazine, which with PhCNS gave the phenylthiourea, m. 94-4.5°; p-nitrobenzylidene derivative m. 90.5-1.5°; treatment of the hydrazine with BzCl gave 1,1-bis[2-(2-pyridyl)ethyl]-2-benzoylhydrazine, m. 137.5°, in 82% yield. Chromatography on Al2O3 in CHCl3 of the mixed hydrazines above also gave some 1,2-benzoyl-1-[2-(2-pyridyl)ethyl]hydrazine-HCl, m. 212-13°. BzCl and mono-2-pyridylethylated hydrazine mixed in 2N NaOH gave 1,2-dibenzoyl-1-[2-(2-pyridyl)ethyl]hydrazine-HCl, m. 206-7°; free base, m. 93-4°. Me2NNH2 and 2-vinylpyridine heated 12 hrs. in the presence of AcOH gave 45.2% 2-[2-(1,1-dimethylhydrazino)ethyl] pyridine (II), b8105-20°, b6 108-11°, n20D 1.5152, d20 0.9902; HCl salt, m. 126.5°; dipicrate, m. 151-2°; phenylthioureide, m. 113°; the hydrazine and Ac2O gave in 2 days an acetyl derivative, b6 152-6°, 1.5160, 1.0530, which gave an HCl salt, m. 183-4°. The higher-boiling fraction gave 1,1-dimethyl-2,2-bis[2-(2-pyridyl)ethyl]hydrazine, b4 182-7°, 1.5468, 1.0553 (bitartrate, m. 55-8°; HCl salt, hygroscopic solid; dipicrate, m. 168-9°. Similarly obtained was 54.5% 4-[2-(1,1-dimethylhydrazino)ethyl]pyridine, b10 127-8°, 1.5159, 0.9898 (di-HCl salt, m. 147-8°; dipicrate, decomposed at 153-4°; phenylthioureide, m. 91.5-2°; acetyl derivative, b6 173-6°, 1.5211, 1.0165, gave a picrate, m. 156-6.5°, and di-HCl salt, m. 184-6°); the reaction also gave 1,1-dimethyl-2,2-bis[2-(4-pyridyl)ethyl]hydrazine, b6 165-90°, 1.5405, --. II and CH2:CHCO2Me heated 1 day in BuOH gave 52.5% 1,1-dimethyl-2-(2-carbomethoxyethyl)-2-[2-(2-pyridyl)ethyl] hydrazine, b6 161-5°, 1.4988, 1.0949 (picrate, m. 106.5-7°). Similarly CH2:CHCN gave the cyanoethylated product, b7 163-8°, 1.5119, 1.0281 (dipicrate, m. 150-50.5°). Heating 2-vinylpyridine with

1,1-dimethyl-2-(2-carbomethoxyethyl)hydrazine in BuOH in the presence of AcOH 1 day gave a crude product b8 140-90°, containing unidentified products. 1-Phenyl-1-[2-(2-pyridyl)ethyl]hydrazine (III) heated with Ac2O in C6H6 1 hr. gave 2-acetyl-1-phenyl-1-[2-(2-pyridyl)ethyl]hydrazine, m. 116-17°, b3 210-20°; treated with BzCl in NaOH, III gave the corresponding 2-benzoyl derivative, m. 159.5-60.5°. III.2HCl, m. 99-107°, is a very hygroscopic solid.

IT 5517-94-2P, 2-Pyrazolin-5-one, 3-methyl-4-[2-(2-pyridyl)ethyl]-
RL: PREP (Preparation)
(preparation of)

RN 5517-94-2 CAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-4-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



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